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ANNALS OF INTERNAL MEDICINE

OFFICIAL PERIODICAL OF THE AMERICAN COLLEGE OF PHYSICIANS

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DEPARTMENT OF REVIEWS

The Journal will make an especial feature of the reviews of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the [illegible] of reviews.

Editor

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Atypical Features of Acute Coronary Occlusion*

By James B. Herrick, *Chicago, Illinois*

WHEN I asked Dr. Means, our General Chairman, if the subject of acute coronary obstruction were not already old and well worn especially in Boston, he replied that he did not think the problem of coronary obstruction had been worked to death in the east. "The patients have died but not the subject which is ever present and very important." So, with this diplomatically worded official encouragement I venture once more to present this topic.

Acute coronary occlusion was formerly regarded as a pathological curiosity. It is now looked upon as a readily recognizable clinical entity of rather frequent occurrence. I am often asked whether the condition is more common now than it used to be. It is difficult to answer this question positively. Some writers think thrombosis in general is more common than formerly. Probably the seemingly greater frequency really means more frequent recognition both by clinicians and pathologists.

One reason for this belief is that as one reviews the literature one is surprised to find how many cases were described many years ago. In 1910 there were published three outstanding articles on this subject, but they attracted little notice. Obratzow and Strascheko clearly described the clinical features showing the possibility of diagnosis during life. They emphasized the status anginosus, and called attention to the resemblance to abdominal surgical affections. Osler's accurate observations were largely lost because the condition was described as an incident in, or a variant form of, angina pectoris. Sternberg's monograph on Partial Aneurysm of the Heart is filled with histories of cases but the emphasis is on the later so-called aneurysmal effects and little attempt is made to depict the clinical onset of the condition. In the same way the earlier masterly work of René Marie on Infarct of the Myocardium, in 1897, was chiefly a contribution to pathology. The reason no more marked impression was made by these papers and by others that preceded them was because the cases were viewed as rarities, as nearly always resulting fatally, and as almost impossible of intra vitam diagnosis; or they were approached from an entirely different avenue than the clinical.

But in the last two decades pathologists and clinicians—and American observers have played a conspicuous part—have paid more attention to the coronary artery, have more critically analyzed cases of angina pectoris,

*Read at the Boston meeting of the College of Physicians, April 10, 1929.

acute dilatation of the heart, heart failure, ptomaine poisoning and acute indigestion, and the importance of obstructive lesions in the coronary artery has been recognized and the clinical features more clearly depicted.

It has often happened that the earlier views concerning a disease have had to be modified as time went on and experience broadened. The clinical picture of exophthalmic goiter of thirty years ago is not that of today, particularly with the help offered by the basal metabolic rate determination. Mild, atypical, bizarre cases are today recognized as associated with faulty thyroid function that then would have been passed as not fitting into the classic syndrome of symptoms. In a similar way our conceptions of acute coronary occlusion are being gradually modified and will be still further altered, for our knowledge of it is far from complete both as to etiology, pathology, clinical manifestations, prognosis and treatment.

In this paper I desire to call attention briefly to a few atypical features of this condition.

By the typical picture is understood something like the following:

The patient, generally an adult who may have known of hypertension or may have had angina pectoris, is seized suddenly, perhaps while quiet, with a severe substernal or upper epigastric pain that may radiate to the neck, arms or epigastrium. Contrary to the rule that holds in attacks of angina of effort the pain does not soon disappear, it lasts and requires large doses of morphin for its relief. There is evidence of shock or collapse, the countenance is ashy, the pulse weak, generally rapid, perhaps irregular, the heart tones faint. The blood pressure falls. Dyspnea may be marked. Death may occur in a very short time or the patient may live days, weeks, or may recover. The heart may show that it has been hard hit, by its persistent weakness or irregularity and by dyspnea, râles, enlarged liver, albuminous and scanty urine. Strongly suggestive are a pericardial friction a few hours or days after the accident due to the roughening of the pericardium over the infarcted area; also a rise in temperature and a leucocytosis. Electrocardiographic changes are quite significant. Such a grouping, when other diseases that might produce similar symptoms can be excluded —such as gall-stones, perforating ulcer, acute pancreatitis, diaphragmatic hernia, pneumothorax—is almost pathognomonic of acute obstruction of the coronary artery.

But not all cases are so classic. In 1912 when I first became interested in this subject I made a tentative grouping as follows:

1. Cases of instantaneous death.

2. Cases of death in a few minutes or hours.

3. Cases of severity, with death deferred for many hours, days or weeks; or at times ending in recovery, i.e. the cases that live long enough to permit of study and that arouse the greater clinical interest. The type of this case I have just described.

4. Cases with mild symptoms.

This latter group I am convinced is far more important than is generally realized. There are, to quote from

what I have written elsewhere[1]: "nonfatal cases with mild symptoms, slight anginal attacks, perhaps without the ordinary causes such as walking. Some of the stitch pains in the precordia may well be due to obstruction of small coronary twigs. Such interpretation of these phenomena, while largely a surmise, is based on the fact that other causes for the pains are lacking and that the patchy fibrosis of the myocardium that is later found at autopsy may have originated in a progressive narrowing of the sclerotic vessels, with, from time to time, acute thrombotic occlusion of small branches; and such obstruction in small vessels may well have produced symptoms differing chiefly in degree from those caused by obstruction of the larger arteries of the heart. Since 1912 when I began looking for these cases of coronary obstruction clinically, I have seen several patients in whom I have felt that such obstruction of small vessels with mild symptoms had occurred. In some instances two or three attacks of mild character differing from the more familiar effort paroxysm of angina pectoris have been followed at some later period by severe and unmistakable symptoms of occlusion of a vessel of larger size. A thrombus in a small branch of the coronary artery may produce mild symptoms just as a clot in a small twig of the cerebral vessels may cause transient and comparatively trifling symptoms very different from the hemiplegia or possibly sudden death that follows the embolic or thrombotic plugging of a vessel more important or of larger size."

Many such cases never come to the doctor; the distress and disturbance are so slight as to be ignored by the patient. Other cases are easily overlooked even when the doctor examines carefully. Breathing, color, heart rate, heart tones, blood pressure, etc., may be apparently unchanged. In some it may be suspected that a coronary accident has occurred, especially if blood pressure can be shown to have fallen a few points, if there be a slight elevation of temperature or increase in polynuclear white blood cells or if the electrocardiogram shows suggestive tracing.

Under this head may perhaps be included attacks when the pain is frankly substernal, quite severe, with short-lived fall in blood pressure, perhaps extrasystoles, with slight elevation of temperature, but in which in forty-eight hours there is an apparent return to normal, no dyspnea, pain or heart irregularity, no fever, with the patient insisting on getting up. He has seemingly recovered.

But some of these apparently mild cases are deceptive and treacherous. A doctor on the third day got up, walked on the street, suddenly dropped dead apparently from ventricular fibrillation. The autopsy showed the obstructing thrombus in the descending branch of the left coronary artery. A woman a few days after a cholecystectomy for gall-stones complains of slight pain in the arms, has dyspnea, rapid pulse, with extrasystoles. In three days she seems better in all respects, dresses her hair herself, laughs and jokes with the surgeon. She is left at ten o'clock

[1]The Weekly Roster and Medical Digest of The Philadelphia County Medical Society, May 23, 1925, p. 15.

at night sound asleep, breathing easily. At one A.M. she is found dead lying on her pillow in an easy position on her side, one arm under her head. A recent thrombus in the descending branch of the left coronary, acute infarct of the myocardium with rupture of the ventricle tell the story.

Some of the patients who have these mild attacks ending in recovery have moreover recurrences in a few days, months or years. Either the thrombus has extended proximally or new thrombi have formed in other vessels.

In most of the descriptions of acute coronary occlusion, pain, usually sudden, is described as an outstanding feature, a pain resembling that of angina of effort, yet often more severe and more persistent, frequently referred to the lower sternal region or to the epigastrium. That this pain should differ in intensity and other characteristics depending on the vessel occluded, its size, e.g. right or left coronary, descending or circumflex branches, or smaller branches,—upon the suddenness or the completeness with which the artery is plugged, is to be expected. So, also, the condition of the coronary system as a whole might materially influence not alone the extent of the infarcted area but the degree of pain experienced. A coronary vessel in which sclerotic changes have been going on for a long time, is often better able to withstand the sudden occlusion because in a compensatory manner collateral vessels have been enlarging as the lumen of the artery in question has been gradually narrowing. Paradoxical as it may seem, a heart with relatively normal coronaries may be less fitted to withstand the insult of a thrombotic closure than the one whose vessels have long been the seat of extensive sclerotic changes. Varying degrees of pain, therefore, might be anticipated because of these varying anatomic conditions present in the heart affected. Such is the case. From the severest pain that resists even large doses of morphine and that lasts for hours or perhaps days throughout a period of status anginosus the pain shades down to milder and milder types until we find instances where there is no pain.

While in my own experience some pain has nearly always been present and generally has been severe, many observers call attention to cases where pain has been absent. Sudden dyspnea, with symptoms of collapse, clammy sweat, nausea, ashy color, and definite drop in blood pressure speak for a cardiovascular accident. The subsequent history showing perhaps a pericardial friction, rise in temperature, leucocytosis, with persistent evidences of cardiac weakness, with typical electrocardiogram tend to confirm the impression of coronary occlusion. Autopsy reveals the obstruction with the myocardial changes. Some regard a suddenly developing dyspnea as a phenomenon more significant than pain. Others stress the abrupt drop in blood pressure. Dyspnea and drop in blood pressure might be spoken of as the pain equivalents of acute coronary occlusion. Is it not better to look upon the *grouping* of symptoms as the surest indication of the accident rather than to overstress the one?

Gallavardin and Gravier[2] regard pain —referring to it as angina pectoris—as playing a secondary rôle in the symptomatology of cardiac infarct. One reason for their view which differs from that of most other observers, is that they are considering not alone the cases of acute coronary obstruction but subacute and chronic as well.

It is clear that we should not stress the symptom of pain too much. We should not, because pain is slight or even lacking, exclude occlusion when other symptoms point to this accident.

Sudden dyspnea has been stated by some to be the regular, invariable accompaniment of this condition. It is of common occurrence. But in some cases it is trifling or entirely lacking. Râles, cyanosis, Cheyne Stokes' breathing, dyspnea, while often present are very variable as to frequency, degree, and time of appearance. They largely depend, one must assume, on the extent to which the heart's efficiency, especially that of the left ventricle, has been interfered with. The easy breathing of some patients whose rapid pulse, feeble heart tones and low blood pressure show marked cardiac weakness has sometimes been a surprise.

More careful and extended observations with post-mortem check may enable us to explain why in some instances dyspnea is marked and in others not. It is to be recalled that some authors, e.g. Pletnew, and Libman have already aimed to distinguish between an infarction in the right heart and one in the left. According to them, dyspnea is more outstanding when there is damage to the myocardium of the left heart.

A marked drop in blood pressure is very significant. Such a drop is particularly helpful in diagnosis when the existence of a previously high pressure is known. But I have seen cases in which the pressure stood up wonderfully well. And another puzzling feature in some instances has been the remarkable daily variations in pressure —a systolic pressure today of 120, tomorrow of 180, etc.

Perhaps after all, these variations are no more to be wondered at than are those of the pulse. Commonly rapid, weak, perhaps with extrasystoles, it may be full, regular, not rapid, or it may show extrasystoles, block, auricular fibrillation. And most extraordinary variations are possible from day to day or even from hour to hour.

One might dwell on other atypical features. Some cases have little or no rise in temperature or even a subnormal temperature. The leucocytes may vary much in number. The radiation of pain may be as variable as in angina of effort. The electrocardiogram may show most remarkable and bizarre pictures with almost unbelievable variations from day to day. The close resemblance of many cases to surgical abdominal accidents has been dwelt upon by many writers. The differential diagnosis is generally easy if this cardiac condition is thought of; but not always. One may at times feel that it is wiser to have an exploratory operation to remove the doubt than to await developments, perhaps by waiting taking from the patient his only hope of recovery by operation. The instructive case recorded by McNee

[2]Gallavardin et Gravier: Formes Cliniques de l' Infarctus du Myocarde, Annales de Med., 1926, Sept., p. 161.

might be cited as a good example. Especially difficult are those cases in which an individual has, let us say, gall-stones or duodenal ulcer and then has an acute coronary occlusion. I know of one instance where in such a case the patient died suddenly during the operation for gall-stones; the autopsy revealed a recent infarct of the myocardium and rupture of the heart. The gall-stones also were there. Which had caused the initial symptoms?

There is only one other point to which I will call attention, though many others might be mentioned. There is a general agreement that the obstruction in these acute cases while occasionally due to an embolus, is usually caused by a thrombus that forms in situ. But in a not inconsiderable proportion of cases embolic phenomena are noted after the accident, at times soon after, at other times many days or even weeks later. The explanation commonly offered is that from the intracardiac thrombus that forms over the site of the infarcted area fragments may be detached and lead to the embolic obstruction of peripheral arteries. If the embolus springs from the right heart the pulmonary artery may be obstructed.

There is another possible explanation for some cases, viz. multiple arterial thromboses. This question deserves further investigation by clinicians, pathologists and experimental workers. The damage to the vessel walls that favors the formation of a thrombus, i.e. the arteriosclerosis and atheromatosis, may be widespread and not limited to the coronaries. There is reason to believe that infection with acute arteritic changes may be a contributing or even determining factor in producing the obstructing thrombus. Unrecognized qualitative or quantitative chemical changes in the blood, or in the number of platelets may be contributing factors. It is conceivable therefore that conditions in the blood with widespread chronic and recent acute changes in the vessel wall may account for the appearance of thrombi not only in the coronary arteries but in others as well. The same question has caused discussion as to the origin of postoperative pulmonary infarction. Generally regarded as embolic, there are those who view the accident as in many instances due to local thrombosis in the pulmonary arteries.

Whatever the explanation in these cases of acute coronary occlusion—and the embolic theory is the best working theory and has much presumptive evidence in its favor—the clinician must be prepared to meet from time to time with evidences of obstruction in other vessels. Emboli in the brain, the kidney, the spleen, the vessels of the leg are occasionally seen—though in my experience rather infrequently. One of the most distressing deaths I have ever witnessed was in a man of sixty with preceding angina of effort, with acute coronary obstruction and the status anginosus. A few hours before death he had most excruciating pain in one leg with disappearance of pulsation in the artery. In another case there was what we regarded as as an acute mesenteric obstruction. Hamman has recently reviewed this feature and cited several instructive cases.

The summary of this fragmentary paper is that our picture of acute coronary occlusion must not be drawn with too fixed lines. We must allow for many variations from the ordinary type, for mild and subacute cases, for cases without pain, for instances of extreme variation in blood pressure, degree of dyspnea, temperature, pulse rate and rhythm. We must be prepared as well for cases with early or late embolic accidents, for recurrences due to proximal increase in the thrombus or to involvement of new vessels. If all this is done the condition will be recognized more frequently even than now and probably a larger percentage of deaths from angina pectoris will be shown to be due to this accident in the coronary artery.

The Failing Heart of Middle Life*

By David Riesman, M.D., Sc.D., *Philadelphia*

MANY men lead active professional and business lives; they may even live reasonably well according to our present standards, but when they reach the age of 50 or thereabouts something happens that was not foreseen by them or by their medical advisors. In ordinary parlance they go to pieces. Upon analysis the disintegration will usually be found due to some change in the heart or circulation. The man who up to the moment of the appearance of the symptoms was active and in the possession of all the energy of the best years of life suddenly becomes an old man.

What is the nature of this process which plays such havoc among useful men, more rarely among women, and in a time of life that we like to call the prime? To be sure there is no definite agreement as to what should be called the prime of life or middle life—youth sets the date early, age postpones it. One day not long ago a student presenting a case before my class began, "Mr. X is a middle-aged man of 40." My heart sank within me. Does middle life begin at 40 or at 50 or, as I like to think, at 55 or 60, partly with reference to the fact that the average span of life has been prolonged to about the age of 56? Women surely are pushing the date farther and farther onward—in dress, in general activity, even in the onset of the menopause, the women of today at 50 are much younger than their mothers were at the same age period. Perhaps instead of taking a particular year, middle life should be dated from a time when a change in function manifests itself from which a beginning wearing down of the machinery can be definitely inferred. Middle life is thus rather a physiologic than a chronologic period.

The disease of the heart to which in the majority of cases the physical breakdown is due is not one affecting the valves—it is as Christian has called it, non-valvular heart disease. Whatever we may know about the clinical manifestations, as to the causes of this condition we are very much in the dark. Sometimes there is an associated hypertension which may be looked upon as the cause. But since we do not know much about the causes of hypertension we are only pushing the problem one step farther back. In other instances the tension is normal or even low. In such cases the changes are usually primary in the heart—a coronary endarteritis or, more often than we think, some functional

*Read before the American College of Physicians, Boston, April 10, 1929.

change for which at present we have no anatomic substratum.

Like Christian (South. Med. Jour., Jan. 1927, p. 28) I have stood more than once in perplexed wonder at the autopsy table when I found an apparently normal heart in a case in which death had been due to cardiac failure. The converse was also not unusual, namely, the finding in a case of accidental death extreme disease of the heart wall though during life there had been no symptoms whatever of a cardiac nature. Such observations prove conclusively that the diseased heart often possesses large factors of safety and suggest that the symptoms are expressions of functional disturbances rather than of anatomic defects.

Failing heart and heart disease are convenient terms, but in their strict meaning they are not sufficiently inclusive. They are largely anatomic concepts—the time has come for a more physiologic interpretation of heart failure. Our conception of the failing heart must encompass the whole circulatory system, including the capillaries. It must also include those obscure metabolic changes arising from defective circulation in the organs and especially in the body musculature.

Some insight into the physiologic disturbances accompanying, or produced by heart disease, is gained through recent biochemical and metabolic studies. Among other things these have shown that in many cases of heart disease there is an increase in the minute-volume of blood and that with improvement, especially under the action of digitalis, there is a diminution of the total circulation, of the minute-blood volume (Harrison and Leonard; Cohn and Stewart). It has been found, furthermore, that owing to an oxygen deficiency in cardiac cases more lactic acid is formed than under normal conditions. While in health a large part of the lactic acid is resynthetized to glycogen, in diseases of the circulation a good deal of the lactic acid formed undergoes destruction by conversion into carbon dioxide and water which entails a distinct loss to the system. Owing to the increased lactic acid production cardiac cases at times present a tendency to acidosis which shows itself in a highly acid urine and in a lowered urinary pH and which may be responsible for certain forms of cardiac dyspnea. To what extent the heart as muscle tissue participates in the altered lactic acid metabolism is not yet known. Many cardiac cases also show a high basal metabolic rate.

The great increase in deaths from heart disease is I believe due to the type of middle life myocardial failure of which I am speaking. Disease of the heart has risen to first place in mortality tables. The Metropolitan Life Insurance Company's statistics for 1928 show a death rate of 143.4 per 100,000 insured, while that from tuberculosis was exactly 90, the lowest ever attained. This marks a drop in tuberculosis of 34.7% during the present decade while the death rate from heart disease has risen from 117.4 in 1921 to the above-mentioned figure. In the United States Registration Area the cardiac mortality was 111.2 per 100,000 in 1910 and nearly 160 in 1924.

To a certain degree the increased death rate from heart disease is not

a debit but a credit, since owing to the enhanced longevity and to the fact that fewer persons die of tuberculosis and other communicable diseases, more individuals reach the age period at which the liability of death from heart disease attains high figures. Nevertheless there is also an actual increase irrespective of the foregoing facts. It is this increase that should be investigated and combated by education of the people and of the medical profession.

When we come to look for the causes of myocardial disease we find certain outstanding facts which while not precisely explanatory of the cause throw considerable light upon the origin of the trouble. Syphilis and rheumatic fever in my experience play only a small part in the myocardial disease coming on at middle life. Worry, overeating, sexual excess, intense ambition and striving for success, in other words, the strenuous life, are antecedent conditions.

Not only overeating, but irregular and hasty eating, and insufficient sleep are important etiologic factors, especially in the lives of professional men. Focal infection in all probability plays a rôle but it is difficult in the majority of cases to trace a direct connection because when a focal infection is discovered it has probably been operative so long that its removal though indicated has but little eeffct. The conclusion is likely to be drawn that the focus played no part in the development of the cardiac disease.

Over-indulgence in exercise is undoubtedly a cause of cardiac damage. There are many whose economic circumstances in early life precluded systematic exercise, but when they get to be 45, 50, or older then are in a position to indulge in golf—some do so with impunity, others pay a heavy penalty. Men who want to take up golf in middle life ought not to do so without a thorough physical examination which ought to be repeated after they have played a little.

The various exciting causes that I have enumerated are operative in the majority of Americans that have reached the mid-period of life. Why do they not all succumb to myocardial or cardiovascular disease? Because something else is required—an underlying condition which is given in a large number of cases by heredity.

Heredity: During the past ten years there has been an evident swing of the pendulum away from the environmental factors in disease, including the micro-organismal agents, toward the constitutional factors. Some perhaps are permitting the pendulum to swing too far but no one who has practiced medicine with an open eye can overlook the fact that the bacterial or other environmental influences are scarcely sufficient by themselves to cause disease, barring of course trauma and semi-traumatic agents, such as poisons and harmful dust.

During the period when Philadelphia was one of the worst typhoid-infected cities in the land, a period coinciding with my early years in practice, I was struck by a singular circumstance in two families of my acquaintance. Nearly every member of the one at some time had typhoid fever, while in the other family, comprising individuals in a number of separate households, there was not a single case of

typhoid fever, although the same contaminated drinking water was consumed by all. That observation it seems to me warrants the conclusion that a constitutional factor protected the second family, that factor being absent in the first; or to put it another way, the members of the typhoid family inherited from generations back a high susceptibility.

Now when we come to study myocardial disease or diseases of the circulation a somewhat similar fact emerges. We find families that seem to be entirely or almost entirely immune to mid-life circulatory diseases. I have gathered statistics of a family related to me by marriage—in two generations there were 56 members all born in Philadelphia and belonging to several different households. Of the 56, 11 have died, not one of myocardial disease. Those living range in age from 40 to 85 years. By contrast I know a family in which two out of four have died of angina pectoris; in another of five members one has died of angina pectoris, another is seriously ill with coronary disease.

The familial circulatory taint need not assume the identical form—it may be angina pectoris in one, coronary thrombosis in another, apoplexy in a third, and ordinary myocardial degeneration in a fourth. When such related diseases affect the same family we are warranted in inferring that a constitutional anomaly exists, a taint of the genotype without which whatever external factors may exist are inoperative or at least incapable of doing the same degree of harm. I shall today not enter into the possible anthropologic features that might lead to a recognition of the abnormal genotype. George Draper, Julius Bauer, F. Kraus and others have indicated the pathways to be followed in this difficult field. What I want to emphasize is the importance of a study of the family history. It will be found that short life is as much an hereditable trait as longevity, which is undoubtedly a family characteristic. That there are exceptions in any given family does not disprove the truth of the statement. I am sure the myocardial disease of middle life of which I am speaking is preeminently a familial or hereditary affair, a fact of which anyone can convince himself by studying the family trees of his patients.

Obesity is another possible etiologic factor. I am not sure whether my experience tallies with that of other men but I have come to believe that the hydrolipemic type, the excessively fatty individual, does not as a rule fall a victim to presenile myocardial disease. It is the overweight solid type, men and women whose fat is firm, who are not very far above the ideal weight, not grotesque in their obesity, among whom we find myocardial disease most frequent. It can not however be said that there is a characteristic physical type liable to myocardial disease. All physiques are met with, the tall and lank, the shortnecked and solid.

Pathology: The actual pathologic conditions vary widely and are, as I have indicated at times, disproportionate to the symptoms during life. Eppinger reports two cases that are of interest in this connection. Both had advanced decompensation, in one the heart at autopsy was markedly dis-

eased, in the other very litle could be found.

Many use the term myocarditis for the diseased condition I am discussing. In a strict sense that word is not always applicable, for the criteria of inflammation are frequently wanting. We meet with the same complication in our nomenclature of kidney affections. Because of the similarity of concepts and of morbid states, I believe we might use the terms myocarditis and myocardosis as we use those of nephritis and nephrosis.

The distribution of myocardial disease is often more important than the type. When it attacks the conductive system, it may produce striking conditions out of proportion to the extent of the lesion. In many instances, in more than is usually imagined, the basis of myocardial disease is an endarteritis of the coronary vessels.

Symptomatology: Patients with myocardial disease present, in the beginning at least, four principal types of symptoms that might be called:

I. The respiratory.
II. The digestive.
III. The painful.
IV. The oppressive.

The respiratory is the most common type. An individual previously well, perhaps fifty or fifty-five years old, experiences shortness of breath on effort or he finds himself seized with paroxysms of air hunger, especially at night, which compel him to sit up and gasp for breath. I have seen this latter type as the very first manifestation of serious structural disease of the heart, in the entire absence of any valvular defect or of any previous suspicion that the heart might be diseased. The patient, and sometimes the physician, attributes the shortness of breath to lack of exercise, to obesity, to indigestion, the last especially if there is considerable gaseous distension. A careful examination in the way I shall later detail will guide the physician to the vitally important correct diagnosis.

Sometimes in addition to a slight shortness of breath the myocardial patient has a racking cough usually out of proportion to the signs found in the lungs. Such patients are looked upon as having chronic bronchitis or asthma, the myocardial cause being overlooked.

II. The digestive type:

This is perhaps the most important to understand as errors in diagnosis are more frequent than under other conditions. Elsewhere I have spoken of the gastric masquerades of myocardial disease (Journal of the American Medical Association, November 17, 1928, Volume 91, 1521). A case report will illustrate this phase of the subject. Mr. T., a successful and somewhat opinionated financier, complained of poor appetite, gaseous distension, constipation and insomnia. His case had been diagnosed as one of stomach and liver trouble and he had been sent to Vichy on the basis of that diagnosis. Under a rigid regime which excluded all meat from the dietary, he lost a good deal of flesh and came back to Philadelphia much worse than he had been. On examination I found a tall spare man of pale sallow complexion with labored breathing, which he said was due to "gas." The heart was markedly enlarged to the left, the liver extended three fingers' breadth below the costal margin. I

placed the patient on a liberal diet and gave him digitalis, a laxative and a mild hypnotic with the result that all his symptoms disappeared, the liver returned to normal size, and he was able about the middle of January to go to Florida.

The gastric disturbances are often so marked—anorexia, nausea, even vomiting—that malignant disease may be suspected and yet the whole syndrome harks back to a myocardial defect.

Failure to make the proper interpretation is usually due to the absence of a cardiac murmur which needs must be present to induce some physicians to diagnose chronic heart disease. Yet there are more non-valvular than valvular cases of chronic heart trouble.

III. The painful type:

Little need be said about the anginal type—the pain, in location, severity and psychic concomitants, is usually suggestive or pathognomonic of cardiac disease. Variations occur, however, and require careful study, particularly those in which the pain is referred to the gall bladder region or to the epigastrium. I have seen quite a number of cases in which it was difficult at first sight to tell whether the patient had angina pectoris or gall-bladder colic. It must also be remembered that chronic cholecystitis or gall stone may in its turn cause cardiac disease.

Under the anginal type I include coronary thrombosis, an increasingly common cause of failure of the heart in middle life. The growing frequency may be due to a better acquaintance with the disease, although I have come to think that there is an absolute increase in cases of coronary occlusion.

IV. The oppressive type:

Perhaps it is not justifiable to make a separate type of this, yet it is sufficiently common and distinctive, although it soon merges with one of the others. The patient on walking experiences a sense of oppression either across the upper or midsternal region or in the epigastrium. If he stops it passes off, sometimes with a little belching, sometimes without any gastric element. The trouble appears to be mild, yet it involves the possibility of sudden death. It has been called angina sine dolore but there is no angor animi and the patient unless he is a doctor rarely considers the symptom significant.

Many persons, especially men of prominence, die according to the newspapers of acute indigestion. The additional statement is often made that the dead man had not complained of heart trouble before. Apart from the probable fact that death was not due to indigestion but to disease of the heart, I always doubt whether the attack was not preceded by symptoms which were of a cardiac nature but were not interpreted either by the patient who failed to have himself examined or by the doctor if an examination was made. To illustrate: Mr. S., 54 years of age, was passed for life insurance for $150,000 one month before I saw him in an attack of coronary thrombosis that ended fatally in 48 hours. When the agent came with the policies he brought policies for an additional $150,000 which the patient declined. Within one month after paying a single premium, Mr. S. was dead.

Now here is the interesting point in the history. It appears that for some time prior to taking out the insurance Mr. S. had complained of a little mid-sternal oppression unaccompanied by pain. He thought it was indigestion or something of that sort, and as he was not seriously handicapped otherwise, he made nothing of it. His blood pressure, urine, and physical condition during the various insurance examinations were all found normal. Of course, when I saw him, his ashen appearance, his low blood pressure, the terrific pain, and the action of the heart all testified to the approaching dissolution. Could such a catastrophe have been foreseen or suspected as a possibility if note had been taken of the oppressive seizures and a more thorough purposive examination had been made? Would it not be well in all such cases, if the physical signs are negative or equivocal, to make an electrocardiographic examination? I am inclined to think that in such a way the insurance companies may save themselves heavy losses and, what is more important, any defects in the patient's mode of life might be corrected.

Common to nearly all forms of myocardial diseases except the anginal are subnormal temperature, a tendency to emaciation, easy fatiguability and a general lack of mental and physical endurance. These symptoms may be associated with emotional instability and a hair-trigger temperament previously not present in the patient.

Neither singly nor in their totality do the aforementioned symptoms justify a diagnosis of myocardial disease, but they suggest such a possibility even if the signs are not conspicuous.

Diagnosis: Aside from the symptoms the diagnosis of myocardial disease is based upon the following objective criteria:

The most important is increase in the size of the heart. This is rarely absent. It is determined:

a. By locating the apex beat by palpation or inspection although this is sometimes impossible because of its faintness.

b. By careful percussion of the cardiac outline. While some clinicians have no faith in percussion for the purpose of determining the cardiac boundaries, I personally believe it is a useful method provided a proper technique is employed, namely, light percussion upon a finger held firmly against the chest wall. The X-ray is the final arbiter in this matter.

Auscultation is less informing. In the early stages when the diagnosis is most essential it may show very little to which exception can be taken. But if one carefully examines such cases he may find a dulling of the first sound at the apex or perhaps a treble sound—an apparent doubling of the first sound—the anapest type of gallop. Such a rhythm in a case presenting an otherwise unexplained dyspnea or failure of strength or ill-defined gastric symptoms is to my mind very suggestive of myocardial disease. This particular change in the heart sounds has helped me many times to a correct differential diagnosis as between a purely gastro-intestinal affection and myocardial disease. I want to emphasize that I am not speaking of the gallop commonly heard in mitral stenosis in which the second sound appears to be split or reduplicated, but

of the one which is more like the canter of a horse, or as I have said, the anapest type of gallop.

What about arrhythmia?

The significance of this abnormality depends somewhat upon the kind but also upon other factors not always discoverable by physical examination. What I have in mind in this connection is the following: A persistent total arrhythmia is indicative of auricular fibrillation but not every case of this gives a serious prognosis; much depends upon associated conditions, particularly upon the presence or absence of mitral valve disease. I know individuals who have lived for years with a constant total arrhythmia and are leading active lives. There may be a small patch of myocardial disease that upsets the rhythm without in any way disturbing the main functions of the heart.

Extrasystoles may be significant yet there are cases in which extracardiac factors, toxic causes, seem to produce the arrhythmia. The heart behaves otherwise in a normal manner.

The blood pressure has no constant characteristics—it may be high and hypertension is perhaps most common, or it may be normal or low. Usually it falls in the coronary thrombosis cases precipitously, in other cases more or less slowly. A considerable fall in a patient who has no pain but either the respiratory, digestive, or oppressive type of symptoms adds to the gravity of the prognosis.

The electrocardiograph as a rule is very helpful in the diagnosis and in the prognosis of myocardial cases, but it may lead us into error. My experience has been that when the instrument reveals myocardial disease then that disease is present. But when the electrocardiogram is negative a serious myocardial affection may nevertheless exist. I have at the present time under observation three patients in whom the electrocardiogram is normal but in whom everything else points to a definite myocardial damage.

While myocardial disease as such produces no murmur, a murmur may be present, which however in no way vitiates the belief that the disease is non-valvular in origin. Such a murmur is often heard at the aortic area and is transmitted upwards to the clavicles over which it is sometimes heard more loudly with a Bowles stethoscope than over the aortic area itself. This murmur is not due to stenosis of the aortic orifice; it may be due to sclerotic changes in the root or arch of the aorta or to dynamic factors conected with an hypertrophied heart or a dilated aortic arch.

A systolic murmur may also be heard at the mitral valve. Many on hearing such a murmur diagnose mitral disease, mitral insufficiency. That is a wrong interpretation if it implies that the murmur or the regurgitation is due to an old valvulitis. The murmur is a secondary feature of no great moment in the diagnosis but of some importance in prognosis, as it indicates a weakening of the mitral ring or is evidence of extension of the sclerotic process to the valve leaflets.

Treatment: When an individual consults his doctor, whether for the purpose of a health examination or for other reasons, the physician should carefully go into the family history and estimate the pathologic load upon

the family tree. The discovery of an inherited taint, especially of the heart and circulation, should lead to regulation of the man's or woman's life in the direction of conserving the integrity of that system.

Foci of infection should be removed if their removal does not entail any undue risk and if a reasonable connection can be conjectured between the infection and the cardiovascular disease.

Perhaps the most important point to bring to the attention of the people in connection with myocardial disease is the desirability of regular physical examinations which the profession has been preaching, but so far with not much success. The public must realize that to pay for a physical examination in apparent health is money well spent.

Treatment must always concern itself not only with the relief of the immediate distress but especially with the prevention of further attacks. The primary essential in treatment is rest—physical and mental. If the evidence indicates definite coronary artery involvement, which, it should be remembered, can exist without causing pain of any sort, then the rest must be absolute and prolonged. Four weeks is the irreducible minimum. During that time the patient must use the bed pan unless as not uncommonly happens, the strain is too great; then the sentence may be commuted to the commode. The doctor must use judgment.

Those in whose families cardiovascular disease has occurred should either not smoke at all or should use tobacco with great moderation.

The meals should be small, especially the evening meal, and the food simply prepared. Unless there are complications, no special dietetic restrictions are necessary except that pastry, fried food, fresh bread, etc., should be omitted.

One of the bugbears of myocardial patients is gas, which is usually attributed to some article of the diet. I have however observed just as much distress, often even more, after a light meal such as a cup of broth, a glass of milk, or even a glass of water as after a mixed meal. Fluids in excess cause discomfort—I limit my patients to 1200 cc., which includes water, milk, broths, orange and other fruit juices, all measured as liquids. There are particular cases that may have to be put on a milk diet or upon butter milk or acidophilus milk for a few days in the beginning of treatment but after improvement, cereals, dry or cooked, with sugar rather than with salt, chicken, chops, oysters, cooked green vegetables, stewed fruit, especially apple sauce, orange juice, thin toast (Melba toast) may be added.

I am very partial to the use of sugar in some form in myocardial cases and sometimes prescribe pure cake chocolate—not milk chocolate.

If patients complain of a bad taste or have a dry tongue I order the chewing of gum, an all too popular habit that I despise in health but encourage in sickness.

If the gas is not controlled by diet, an enema will usually give relief. Hot compresses, flaxseed poultices, the rectal tube, pituitrin are measures to combat the severer cases of distension.

Insomnia is often the most distressing of all symptoms. Sometimes the bromids suffice although usually stronger remedies must be given—allonal, medinal, etc. But in the majority of cases nothing is so helpful as the opiates, preferably codein, but there should be no hesitation in giving morphin sulphate hypodermically in grains ⅛ to ¼ with a little atropin. When morphin is used there is of course some danger of habituation but by gradually reducing the dose or occasionally substituting distilled water one can guard against this.

Digitalis: In the severe coronary cases I prefer to wait with the use of digitalis until the hyperacute symptoms have abated. Then and in other myocardial cases from the beginning digitalis may be given in moderate doses. It will be found beneficial whether fibrillation exists or not. I shall not say much about the other cardiac stimulants except that my preference is for caffein sodiobenzoate.

Psychotherapy: This is the most important part of the treatment. In no condition is the influence of mind over matter so clearly exhibited. An encouraging word or gesture makes the patient eat and sleep better with all the good results that ensue therefrom.

Nauheim Treatment: I have seen good results from treatment at spas, especially Nauheim, and from similar treatment at home. It is unnecessary however to go into details.

Exercise: In the severe cases, especially in those dependent upon coronary disease, exercise is forbidden for a long time. As Sir Clifford Allbutt has said, "The patient must crawl before he can walk." The passion for golf often drives men to over-exert themselves, to do more than the circulation can stand.

The first thing the patient does when he is better is to sit up in bed, then he sits in a chair for increasing periods, then he takes short level walks, then a motor ride of one hour from room back to room, then longer walks and rides, then lastly, a little golf on a non-hilly course.

By such measures many a man who has shown definite physical and electrocardiographic evidence of myocardial disease may be restored to health and usefulness. But if he has offended nature he must be told as a final injunction, "Go and sin no more."

Undulant Fever in the United States*

By George Blumer, *New Haven, Connecticut*

It is the purpose of this paper to discuss the following aspects of the problem of undulant fever in the continental United States: (1) its incidence and distribution, (2) its origin and (3) the best methods for its detection.

The Incidence and Distribution of Undulant Fever

The incidence and distribution of undulant fever in the continental United States, so far as this can be discovered from the literature and by correspondence with state health departments, is shown by the accompanying spot map (Fig. 1). Before discussing this map it must be explained, first, that no reports were received from the states of Oklahoma and Tennessee and second, that in the states of Alabama, Arkansas, Colorado, Idaho, New Hampshire, Rhode Island, West Virginia and Wyoming no cases had been reported or come to the knowledge of the State Department of Health. Inasmuch as the disease is not a reportable one in many of these states this must certainly not be regarded as evidence that the disease does not exist in them. It can hardly be doubted that it occurs in every state in the union. It should also be noted that in the map cases are credited, when that is possible, to their place of origin rather than to the place where a diagnosis was made. It is not claimed that the map is absolutely accurate but it is at least approximately so and it is certainly accurate enough to serve as a basis for comment and discussion. The map shows that up to date reports are available of 856 cases in the continental United States, distributed as noted in Table 1.

*Read before the American College of Physicians, Boston, April , 1929.

Table I

Undulant Fever Cases by States

Arizona	69	Iowa	162	Mississippi	3	Ohio	20
California	29	Kansas	17	Missouri	31	Oregon	13
Connecticut	18	Kentucky	43	Montana	2	Pennsylvania	22
Delaware	3	Louisiana	1	Nevada	3	South Carolina	2
Dist. of Columbia	5	Maine	9	New Jersey	3	South Dakota	2
Florida	1	Maryland	13	New Mexico	18	Texas	62
Georgia	37	Massachusetts	2	New York	76	Utah	8
Illinois	33	Michigan	73	North Carolina	3	Vermont	3
Indiana	32	Minnesota	20	North Dakota	4	Virginia	5
						Washington	3
						Wisconsin	6

MAINE
VERMONT
NEW HAMPSHIRE
MASSACHUSETTS
RHODE ISLAND
CONN.
NEW YORK
NEW JERSEY
PENNSYLVANIA
MARYLAND
DELAWARE
VIRGINIA
WEST VIRGINIA
NORTH CAROLINA
SOUTH CAROLINA
GEORGIA
FLORIDA
ALABAMA
MISSISSIPPI
LOUISIANA
TEXAS
OHIO
KENTUCKY
TENNESSEE
MICHIGAN
INDIANA
ILLINOIS
WISCONSIN
MINNESOTA
IOWA
MISSOURI
ARKANSAS
OKLAHOMA
KANSAS
NEBRASKA
SOUTH DAKOTA
NORTH DAKOTA
COLORADO
WYOMING
NEW MEXICO
UTAH
ARIZONA
MONTANA
IDAHO
NEVADA
OREGON
CALIFORNIA
WASHINGTON
UNDULANT FEVER IN THE UNITED STATES

Several things can be noted from a study of the map, of which the following are perhaps the most important:

(1) That there are large areas in the country from which no cases have been reported.

(2) That there is a permanent local focus of goat infection in Texas.

(3) That the extent of infection in those states from which the disease is reported varies greatly.

(4) That in heavily infected states such, for example, as Iowa or New York, the disease is widely disseminated and occurs both in the country districts and in large cities.

(5) That, in addition to isolated cases, family outbreaks and institutional outbreaks, though uncommon, have occurred. The only real city outbreak was that at Phoenix, Arizona, in 1922, from infected goat's milk. It is permissible, we think, to speak of state-wide outbreaks in Iowa, New York and Michigan.

With regard to the states from which no cases have been reported, it is to be noted, as remarked above, that the disease is a non-reportable one in many of them. However, in other states where the disease is also non-reportable cases have been detected and have been recorded in the literature. We can hardly assume, I think, that any one state or group of states has any monopoly of physicians who are unaware of the existence of the disease, and who overlook it. It is undoubtedly true that some health departments and some physicians are more keenly alive to the possible existence of the disease in their territory than others. In some states the routine testing of sera sent in for the Widal or Wassermann tests has led to the detection of unsuspected cases and has stimulated interest in the disease.

The disease as originally described, i.e. as a goat-transmitted infection, has existed in Texas for at least forty years. In their 1911 report Gentry and Ferenbaugh state that it had then been known in Edwards County for twenty-five years. Foci connected with the goat raising industry have also been known for many years in certain parts of Arizona and New Mexico and it is to be expected that undulant fever of caprine origin will be found wherever goat raising is a prominent industry. (See Table 2.)

TABLE 2

Number of Goats in States having over 1,000

Texas	1,791,325	Utah	48,292	Nebraska	2,952
Arizona	281,564	Florida	36,944	Wisconsin	2,893
New Mexico	240,067	Kentucky	33,255	New York	2,542
Oregon	21,193	Oklahoma	32,436	Minnesota	2,082
Missouri	118,316	Colorado	21,525	Ohio	2,001
California	98,859	South Carolina	16,395	Idaho	1,602
Arkansas	95,731	North Carolina	15,959	Pennsylvania	1,536
Georgia	90,606	Virginia	5,774	Montana	1,475
Alabama	72,469	Washington	5,586	South Dakota	1,396
Mississippi	64,947	Kansas	5,581	Wyoming	1,152
Tennessee	63,154	Iowa	5,435	North Dakota	1,064
Louisiana	59,767	Indiana	3,995	Michigan	1,015
		West Virginia	3,994		

The variable extent of the disease in different states will probably not be satisfactorily explained until we have more exact knowledge of its origin and the method or methods of its transmission. It is clear that in most infected states it is entirely independent of the goat-raising industry and we may at once discuss as satisfactorily proven the caprine origin of certain groups of cases and concentrate our attention on those cases which are not due to goat's milk or its products. It is proper also to place in the category of proven cases those occupational ones of porcine origin which occur among slaughter-house employees and laboratory infections in bacteriologists. From an epidemiological viewpoint it is the cases which are now quite generally assumed to be due to cow's milk infected with the B. abortus type of organism which should claim our attention.

The Origin of Undulant Fever in the United States

We have already stated that there are two groups of cases concerning the origin of which no doubt exists: (1) the group associated with the goat-raising industry, (2) the occupational groups of porcine or laboratory origin. It has been quite generally assumed by health authorities that cases not of caprine or porcine origin are due to the transmission through cow's milk of the abortus type of Brucella originally described by Bang of Copenhagen and referred to in the older literature as the *Bacillus abortus* of Bang. Anyone who has read the literature carefully must have been struck by the fact that decisive proof that the milk of cattle suffering from contagious abortion can transmit undulant fever to man is lacking in many instances. We shall attempt to state and evaluate some of the known facts for and against the transmission of undulant fever by infected cow's milk.

1. It is known that contagious abortion among cattle is a disease which is widespread throughout many parts of this country. (See Table 3.) Exact information as to its prevalence in some states is lacking but there is enough evidence to clearly demonstrate that, allowing for the sterilizing effect of pasteurization, a considerable proportion of the market milk of many states is contaminated with living Brucella abortus of the bovine type.

2. It is known that undulant fever is least comon among those members of the community who drink the largest amount of milk, namely, children. In Denmark, where an analogous situation exists, Madsen states: "No case has ever been observed in the hospitals and the asylums for children in Copenhagen or elsewhere where raw milk is used in large quantities."

3. The actual experiment of feeding healthy individuals with milk known to be infected with bovine Brucella abortus has been made with negative results. In the experiments of Cooledge a feeding test was conducted with six people, none of whom contracted undulant fever. In contrast to this observation it is pertinent to note that cultures of the organism from human beings are very dangerous and that several of the most prominent students of the bacteriology of the disease have developed laboratory infections.

TABLE 3

Occurrence of Infectious Abortion Among Dairy Herds

California	Some herds heavily infected
Connecticut	About 90% of herds infected
Florida	A considerable amount of infection
Georgia	Infection of herds quite common
Indiana	50% of herds infected
Iowa	Infected herds common
Maine	60-80% of herds infected
Massachusetts	Widespread heavy infection of herds
Minnesota	Infection of dairy herds present
Michigan	Infection prevalent
New Hampshire	Large incidence of infection
New York	Estimated that 30% of herds are infected
Ohio	Widespread infection of dairy herds
Oregon	Infection widespread
Pennsylvania	Infection of herds fairly prevalent
Vermont	75% of herds infected
Washington	2.5 to 5% of herds infected

Against these negative observations one must place certain apparently positive ones. For example, the report made by Dr. G. E. Atwood, Health Officer of Waycross, Georgia, of six cases of undulant fever in one family all supplied by the milk of one cow which died of some unknown disease before its blood or milk could be tested. Even where the chain of circumstances is seemingly as obvious as this, however, it must be remembered that the mere fact that infection through cow's milk is generally regarded as probable may have led to the overlooking of some other source of infection.

The real difficulty in deciding the type of infecting organism is a bacteriological one. It is often a simple matter to prove that an individual is infected with an organism of the *Brucella* group, but it is much more difficult to decide which particular member of the group is responsible. There is no question as to the pathogenicity of the caprine type (Brucella melitensis*). The difficulty lies in distinguishing the bovine from the porcine type. As Blake and Oard have pointed out there are three methods of doing this: (1) the guinea pig inoculation test (Theobald Smith, (2) the agglutinin absorption test (Alice Evans), and (3) the bacterial metabolic tests (McAlpine and Slanetz). It is noteworthy that but few organisms isolated from human cases have been submitted to all three tests. Such evidence as exists at the present time regarding the pathogenicity for man of the bovine and porcine types of Brucella abortus suggests very strongly that it is the porcine type which is responsible, even in those cases which appear to be transmitted by cow's milk. In a recent letter Theobald Smith

*The bacteriological nomenclature of the group is in a state of confusion because different bacteriologists have adopted different classifications. In this paper Brucella melitensis refers to the caprine type. The other two types are referred to as Brucella abortus (bovine) and Brucella abortus (porcine).

says: "I may say that thus far none of the twenty-five or more cultures from human beings in this country which I have studied are precisely like the bovine type." To this evidence we may add that of McAlpine and Slanetz, who state that all organisms of human origin which they have studied have proven to be of the porcine type.

unwise in the present state of our knowledge to draw the definite conclusion that most of the recent cases of undulant fever are due to Brucella abortus of the porcine type.

There are other factors which must certainly be taken into consideration. There is always the possibility that Brucella abortus of the bovine type

TABLE 4*

States in which there are over 1,000,000 *Hogs*, 1928

Iowa	10,650,000	Indiana	2,227,000	Texas	1,375,000
Illinois	5,039,000	South Dakota	2,445,000	Oklahoma	1,104,000
Missouri	4,720,000	Kansas	2,320,000	Arkansas	1,088,000
Ohio	2,537,000	Wisconsin	1,863,000	Tennessee	1,084,000
Minnesota	3,710,000	Georgia	1,424,000	Kentucky	1,081,000

*Year Book of Agriculture, 1927.

We are forced to conclude that up to the present, at least, there has not been sufficient study of the origin of undulant fever, which is not of caprine or occupational origin, to enable us to reach a definite decision as to the source of the infecting organism. The small amount of accurate evidence now in existence definitely points towards the porcine type of Brucella abortus rather than the bovine type. This does not eliminate cow's milk as a source of infection for the reason that cattle as well as man may be infected by the porcine type of Brucella abortus. The obvious suggestion which this fact carries is that where undulant fever is transmitted to man through infected cow's milk the cattle have been infected with the porcine type of organism rather than with the ordinary bovine type. It is perhaps significant that the largest number of reported cases have come from the state of Iowa, which is notoriously a hog-raising state. However, it would be

may, in certain localities, have taken on increased pathogenicity, a phenomenon often observed in conection with epidemics of bacterial disease, though not yet satisfactorily explained. The decided increase in recent years of infectious abortion in cattle, pointed out by Mohler, suggests this possibility. Indeed, in view of the rapid increase in the number of human cases reported within the past three years we are justified in suspecting that such a phenomenon is now taking place. It is questionable whether this comparatively sudden increase in the number of reported cases of undulant fever can be explained solely on the ground that the profession and health departments have become more acutely aware of the disease.

CLINICAL DETECTION OF UNDULANT FEVER

As one of our surgical colleagues recently remarked "the key which opens the door of diagnosis is suspi-

cion." Practitioners have always met with obscure fevers. In the older books these are often described under the vague heading of febricula. As new febrile diseases are discovered the number of cases of obscure fever should diminish. We should be suspicious that any unexplained fever, especialy if it assumes an undulant type, is undulant fever. Even in the case of single attacks of fever of comparatively brief duration we should think of undulant fever because there is a mild, often ambulatory, type of the disease in which only a single bout of fever occurs.

A point which has struck the writer in the limited number of cases he has seen is the singular lack of discomfort which some of these patients exhibit. They appear to be able to attend to their ordinary work, at any rate in the earlier weeks of the disease, when they are carrying a fever which would ordinarily interfere with such duties. Furthermore, particularly in the early stages, there is a singular lack of physical signs in many of the patients. In the prolonged cases this ceases to be true in the later stages.

The most satisfactory method of diagnosis is the recovery of some type of Brucella from the circulating blood. The blood should be taken during a febrile period and preferably at the height of a paroxysm. The culture should be observed for a long period. The ordinary routine of many bacteriological laboratories whereby cultures are discarded as negative after three or four days will certainly result in the overlooking of some cases. In view of what has been said in the preceding discussion it is important that where organisms are isolated they should be submitted to a skilled bacteriologist and an attempt should be made to determine the exact strain of the Brucella which is present. At times the organism can be isolated from the urine without difficulty, so that urinary cultures are always worth while in doubtful fever cases.

Lacking blood cultures the agglutination test done under proper precautions is of great value. In childhood the blood of a small proportion of individuals contains agglutinins which act in titres as high as 1:300. Several serologists state also that the blood serum of adults may cause agglutination in titres as high as 1:160, even when there is no history remotely suggesting undulant fever. It is thought that these reactions may possibly occur as a result of the ingestion of Brucella abortus in cow's milk. Evans suggests that the reaction is a specific response, while other writers think that the phenomenon is one of passive immunity. Whatever the explanation may be these observations make it clear that agglutination by serum in low dilution cannot be regarded as proof of the presence of undulant fever. The titre of agglutination must be a high one before it is regarded as satisfactory evidence of the presence of the disease.

Conclusion

It is apparent that there has been an increasingly large number of cases of undulant fever reported in the United States during the past two or three years and it cannot be positively asserted that this increase is entirely due to an awakening on the part of health authorities and physicians to the fact that this disease is to be considered in

the diagnosis of obscure fevers. This increase in reported cases of undulant fever has not occurred in the group of cases which are connected with the goat industry. Two small groups of occupational cases of porcine or human origin occurring in slaughterhouse employees and laboratory workers have been split off from the main group, but the great majority of cases recently reported have occurred in individuals who were not obviously in contact with either goats or hogs. The bacteriological evidence as to the origin of these cases is incomplete but definitely points to a porcine rather than a bovine origin, and inasmuch as cattle are susceptible to infection with the porcine type of Brucella abortus the evidence suggests the possibility that cow's milk can, under certain circumstances, transmit the disease. There is need for more careful bacteriological and epidemiological study of the disease. If, as now seems possible, the disease is really on the increase, it will be necessary, in order to control it, to obtain accurate knowledge as to its method of spread. It is also important to determine this, lest, in their enthusiasm, state legislatures begin to pass unwise laws relating to infected cattle and to the distribution or handling of milk and milk products.

REFERENCES*

*Many references are to be found in the article of Kern, Am. Jour. Med. Soc., 128, *175*, 405. Those listed here are not found in this article.

Anderson, J. F.: Hyg. Lab'y. Bulletin, No. 41, 1908, 45.

Arnold, L. and Miller, W. E., Proc. Soc. Exper. Biol., 1926-7, *24*, 836.

Awe, C. D. and Palmer, H. D., Am. Jour. Med. Sci., 1928, *176*, 837.

Blake, F. G. and Oard, H. C., Yale Jour. Biol. and Med., 1929, *1*, 128.

Coffin, C. J. and Famulener, L. W., Proc. New York Path. Socy., 1923, *23*, 150.

Cooledge, L. H., Jour. Med. Res., 1916, *34*, 459.

Corpening, A., Virginia Med. Monthly, 1928, *55*, 254.

Craig, C. F., Internat. Clin., 1906, 15 Ser., *4*, 89.

Dalton, Charles F., New Eng. Jour. Med., 1928, *199*, 837.

Duffee, D. H., Jour. Am. Med. Assn., 1926, *87*, 1830.

Ecker, C. E. and Simon, M.A., Jour. Infect. Dis., 1929, *44*, 62.

Evans, Alice C., Jour. Am. Med. Assn., 1927, *88*, 630.

Evans, Alice C., Pub. Health Rep., 1924, *39*, 501.

Evans, Alice C., Pub. Health Rep., 1924, Rep. No. 906.

Fensen, M. L. and Meyer, K. F., Jour. Inf. Dis., 1920, *27*, 173.

Ferenbaugh, T. L., Jour. Am. Med. Assn., 1911, *57*, 730.

Gentry, E. R. and Ferenbaugh, T. L., Jour. Am. Med. Assn., 1911, *57*, 889 and 1911, *57*, 1045.

Gilbert, Ruth and Brooks, P. B., New York State Jour. Med., 1926, *26*, 1035.

Gilbert, R. and Coleman, M.B., Jour. Infect. Dis., 1928, *43*, 273.

Gillen, H. B. and Gordinier, H. C., New York State Jour. Med., 1928, *28*, 581.

Habein, H. C., Proc. Staff Meetings Mayo Clinic, 1927, *2*, 141.

Hardy, A. V., Pub. Health Rep., 1928, Rep. 1212, also personal communication, March 1929.

Health News, New York State Dept. of Health, 1928, *5*, 49.

King, W. F., Jour. Am. Med. Assn., 1928, *91*, 552.

Lake, G. C., Pub. Health Rep., 1922, *37*, 2895.

Magath, T. B., Med. Clin. N. Amer., 1928, *11*, 1661.

McAlpine, J. G. and Slanetz, C. A., Jour. Infect. Dis., 1928, *42*, 66 and 73, and

16th Amer. Rep. Internat. Assn. of Dairy and Milk Inspectors.
MOHLER, J. R. and EICHORN, A., Jour. Am. Med. Assn., 1912, *58*, 1107.
MURDOCK, T. P. and HALL, W. E., Ann. Int. Med., 1928, *2*, 545.
ORR, P. F. and HUDDLESTON, J. F., Am. Jour. Pub. Health, 1927, *17*, 1242.
PLUMMER, W. A., Proc. Staff Meetings Mayo Clinic, 1927, *2*, 108.
SENSENICH, R. L. and GIORDANO, A. S., Jour. Am. Med. Assn., 1928, *90*, 1782.
SMITH, THEOBALD, Jour. Exper. Med., 1926, *43*, 207.
TAPPAN, J. W., Texas State Jour. Med., 1923, *19*, 176.
TYNDALE, W. R. and VIKO, C. E., Jour. Am. Med. Assn., 1923, *81*, 1953.
WARREN, C. W., SMITH, G. and LINDNER, M. B., Clifton Med. Bull., 1926, *12*, 125.
WATKINS, W. W. and LAKE, G. C., Jour. Am. Med. Assn., 1927, *89*, 1581.
WELLMAN, C., EUSTIS, A. and SCHOCHET, S. S., Amer. Jour. Trop. Dis., 1913, *1*, 393.
WOODWARD, L. R., Jour. Iowa State Med. Soc., 1927, *17*, 312.
WOOLSEY, R. A., Jour. Missouri State Med. Assn., 1918, *15*, 164.
YOUNT, C. E., Mil. Surg., 1913, *33*, 540.
YOUNT, C. E. and LOONEY, R. N., So. Cal. Pract., 1912, *27*, 257.

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Pernicious Anemia as a Deficiency Disease*

By Randolph West, *Medical Clinic Columbia University and Presbyterian Hospital, New York*

In discussing the nature of Pernicious Anemia, we wish to confine ourselves strictly to the idiopathic anemia described by Addison and later by Biermer, and differentiate it as sharply as possible from other anemias with similar blood pictures.

In Addisonian Anemia three organ systems are dominantly affected, the gastro-intestinal tract, the blood, and the central nervous system.

The lesions in the gastrointestinal tract are glossitis, and an achylia gastrica associated with an atrophy of the gastric mucosa. Both pepsin and HCl are lacking in the gastric secretions, and injections of histamine do not lead to any secretion of acid as is the case in functional achylias. Levine and Ladd,[1] in analyzing 122 cases of Addison's anemia, have found but one case that failed to show achylia, and other workers have found this association so constant that it is now felt that achylia is a necessary finding in making the diagnosis of Pernicious Anemia. More interesting still are reports by Levine and Ladd, Hurst,[2] Wilkinson[3] and others that achylia had existed, 10, 13 and even 20 years before the anemia developed. In this connection Hartman[4] and Sir Barclay Moynihan[5] have reported the development of a pernicious anemia blood picture following total gastrectomy. Finally, all reports to date agree that with the liver diet, while the blood improves dramatically and the cord symptoms improve somewhat or are arrested, the achylia persists unaltered. The achylia then, is invariably associated with the disease, antedates it in time, and persists after the return of the blood picture to normal.

The blood picture consisting of a marked reduction in red cells, high color index, megalocytosis, poikilocytosis, leukopenia and reduction of platelets is well known, while the high serum bilirubin, the increased excretion of urobilin in stools and urine, and the marked deposits of hemosiderin in the liver, spleen and kidneys are the classic arguments in favor of a hemolytic anemia. The blood cholesterol is also reduced,[6] and the red cells slightly less fragile than normal.

Of greater interest than the peripheral blood are the findings in the bone marrow. The constant autopsy finding of replacement of the fatty marrow of the long bones with red marrow very rich in megaloblasts has been extended by the observations of Peabody.[7] By trephining the tibia he was able to observe the marrow from the most

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severe stages of the disease through to remission. As the condition of the patient and the peripheral blood picture improved the marrow picture changed from the megaloblastic hyperplastic marrow to the normal adult fatty marrow. Megaloblastic hypertrophic marrow coincided with relapse, normal marrow with remission, and these changes follow the institution of liver diet or potent liver extracts. The outpouring of reticulocytes which had been observed in the pre-liver era before spontaneous remissions, has been shown by Minot[8] and his colleagues to occur regularly about a week after beginning the liver diet, and the feeding of liver in some way enables a hyperplastic marrow filled with megaloblasts to convert these immature red cells into mature forms which enter the peripheral circulation. Whether this is done by neutralizing an hypothetical toxin or supplying missing building blocks will be considered shortly. Coincident with the blood and marrow improvement just mentioned, serum bilirubin, urobilin in stool and urine, and blood cholesterol return to normal. It is also interesting that in those cases having edema, a diuresis occurs shortly after the liver diet is started.

The changes in the central nervous system may occur with the anemia or alone; they are always, however, associated with achylia. The essential lesion, according to Collier,[7] is a primary degeneration of the myelin sheath, with no glia reaction. The tracts most often affected are the dorsal columns and the pyramidal tracts with the usual symptoms of loss of function of these pathways. There are in addition scattered patches of degeneration of the white matter throughout the cord and brain itself. In the great majority of cases the cord lesions are usually arrested, and in some instances markedly improved by the liver diet.

Such in brief are the pathological changes encountered in Addison's anemia, and their response to liver therapy. One other point may bear on the nature of the disease, its racial distribution. It is largely a disease of the so-called Nordic races, and is most prevalent in the Scandinavian countries, Great Britain, Germany, Canada and the United States. It is almost unknown in China, South America and Java. Draper[10] has found that on measuring pernicious anemia patients anthropologically that these measurements correspond closely to "eunuchoid" type, and that the pernicious anemia group have more nearly similar anthropological measurements than any other disease group that he has studied. This points toward a constitutional factor in this disease, and it is not impossible that the omnipresent achylia may be on a constitutional basis.

The nature of the active substance in liver also throws some light on the nature of the disease. The Lilly Extract, which produces all the effects on the blood that have been noted for whole liver, as prepared by Cohn's method[11] is essentially a watery extract of liver, with the proteins removed by heating to 80° in acid solution. The active material is then carried down with the precipitate on pouring into very concentrated alcoholic solution. Further chemical studies carried

out at Harvard and Columbia[12] have agreed in essential points. The active material is not precipitated by sodium sulphate nor basic lead acetate, but is precipitated by phosphotungstic acid and can be regenerated with baryta. From this point on evidence has been obtained that the material is not precipitated by alkaline silver solutions, and that by appropriately fractioning with acetone a biuret negative material can be obtained which is active. We appear to be dealing with an organic base, not precipitable by silver, at least in impure solutions. Of the pure substances that might have been in the best fractions the following have been fed to patients with negative results: spermine, ergothioniene, choline, histamine, histidine.

The best fractions have been effective in doses of about a gram daily, and once half a gram gave a good response. P. has been absent, and N about 12%. Fe is absent.

McCann[13] has fed liver ash in 4 gm. doses daily with negative results.

We have then a mixture of organic bases effective in the doses mentioned.

Most important experiments as to the nature of the disease are those of Castle[14] of Boston. He has found that cases of pernicious anemia did not improve on a diet containing a half pound of lean meat (muscle) daily, but that when the meat was first eaten by a normal individual, regurgitated after 30 minutes, then incubated with HCl for two hours and fed by stomach tube daily, the response of reticulocytes and the rest of the blood picture was similar to that obtained with liver. This is very strong evidence in favor of the view that the gastric digestion of muscle liberates a substance which exists free in liver and kidney, and which is an essential building block for red cells.

For many years upper intestinal sepsis secondary to achylia has been held responsible for the hypothetical toxin of Addison's anemia. Recently Morton, Kahn, and Torry,[15] have produced an anemia in rabbits by injecting the marrow cavity with B. Welchii toxin. The blood picture has resembled that of pernicious anemia and was improved by liver extract. Several years ago we gave a man suffering with pernicious anemia 200 of B. Welchii antitoxin, and his serum contained circulating antitoxin for two weeks, protecting mice from death and red cells from hemolysis with known B. Welchii toxin. There was, however, no improvement in his blood picture nor general condition.

Ashford[16] and others have reported improvement in the anemia of tropical sprue on liver extract. We too have observed the reticuloyte response with a liver fraction in a case of sprue anemia with adequate gastric HCl, and most interestingly Ashford has noted a reticulocyte response from 1 to 10% with R.B.C. at 1 million on a *meat* diet in a sprue patient with HCl in the stomach. It seems possible that the pancreatic digestive disturbance in sprue may in some way function analogously to the gastric fault in pernicious anemia as etiologic factor in the anemia.

Response of Bothriocephalus anemia to the liver diet is cited by Syderhelm[17] as evidence that the liver diet works by neutralizing a hypothetical toxin. The explanation of the results in this

anemia can only be answered by further investigation.

We have observed two cases of Laennec's cirrhosis of the liver with a secondary anemia of 1.5 million red cells each of whom had a reticulocyte rise from 2 to 12% on liver extract. The explanation is obscure. There was acid in the stomach of one, the other had no gastric analysis.

Peabody concluded, after his bone marrow studies that "the course of the anemia" appeared to be "an abnormal type of cell growth consisting in the development of the primitive myeloblast and a failure of differentiation into more mature cells that normally go into the blood."

Minot has shown that the feeding of liver is followed by the appearance of reticulocytes and then mature cells in the blood. Cohn has shown that a gram or so of organic bases from liver a day will accomplish this, and Castle that lean meat, itself ineffective, will accomplish the same result after digestion in a normal stomach. This evidence places the burden of proof on those denying the hypothesis that pernicious anemia is a unique deficiency disease, secondary to a fault in gastric digestion, and that the active substance which is necessary for the maturation of the megaloblast, while free in liver, exists in a combined form in muscle, and probably many other sources. The high urobilin excretion, and organ hemosiderin, are better interpreted as excess of hemoglobin building material which cannot be utilized by an imperfectly functioning bone marrow, than as an evidence of blood destruction. Other anemias known to be due to blood destruction are accompanied by reticulocytosis; pernicious anemia is not until a gram or so of hepatic bases are supplied daily.

It seems, therefore, that there is a substance free in liver, and freed by gastric digestion in meats and probably other foodstuffs, which is necessary for the formation of adult red blood cells, and that the lack of this substance due to faulty gastric digestion gives rise to the picture of pernicious anemia.

REFERENCES

[1]Levine and Ladd: Pernicious anemia. Johns Hopkins Hospital Bulletins, 1921, XXXII, 254.

[2]Hurst: Lancet, 1925, I, 255.

[3]Wilkinson: Cited by Feber and Nyfeldt. Anämie und Intestinaltractus. Ergebnisse der gesamten Medizin, 1928, XI, 273.

[4]Hartman: Blood changes in a gastrectomized patient simulating those in pernicious anemia. Am. J. Med. Sc., 1921, August.

[5]Moynihan: A case of complete gastrectomy. Lancet, 1911, XI, 430.

[6]Muller, Goode, Castle and Rose: Relation of cholesterol and lecithin to remission in pernicious anemia. Proc. Soc. Exp. Biol. and Med., XXV, 567, 1927.

[7]Peabody: Am. J. Path., 1927, III, 197.

[8]Minot, Cohn, Murphy and Lawson: The treatment of pernicious anaemia with liver extract. Effects upon the productions of immature and mature red blood corpuscles. Am. J. Med. Sci., 1928, CLXXV, 599.

[9]Collier: Oxford Medicine.

[10]Draper: Human Constitution (Saunders, Phila.), 1924.

[11]Cohn, Minot, Alles and Salter: The nature of the material in liver effective in pernicious anemia. II. J. Biol. Chem., 1928, LXXVII, 325.

[12]Liver Fractions in Pernicious Anemia: WEST and NICHOLS, J. A. M. A., 1928, XCI, 867.

[13]MCCANN and ELDER: Effect of liver ash on blood regeneration in pernicious anemia. Proc. Soc. Exp. Biol. and Med., 25, 747.

[14]CASTLE and LOCKE: Observations on the etiological relationship of achylia gastrica to pernicious anemia. Read at the meeting of the American Society for Clinical Investigation, Washington, April, 1928.

[15]MORTON, KAHN and TORREY: A pernicious anemia-like blood condition produced in monkeys with bacterium Welchii toxin. Proceedings of the Society for Experimental Biology and Medicine, 1925, XXIII, 8.

[16]ASHFORD: Evaluation of liver extract in treatment of anemias of sprue. J.A.M.A., 1928, XCI, 242.

[17]SYDERHELM: Die Behandlung der perniziözen Anämie. Verhandlungen der Deutschen Gessellschaft für Innere Medizin, 1928, 315.

The Significance of Glycosuria*†

By James E. Paullin, M.D., *Atlanta, Georgia*

WHEN a reducing substance is found in the urine during the course of a routine physical examination, or a patient states that such a substance has previously been found, two questions immediately present themselves for solution: (1) Is the reducing substance glucose? (2) If it is glucose, what condition is responsible for its presence? Upon a correct solution of these problems depends the future welfare and comfort of the patient. It is the purpose of this paper to discuss briefly some of the procedures which are useful in answering these questions.

For several years there has been quite a discussion as to whether human urine normally contains glucose. The statement of Baish[1] in 1895 that normal human urine contained a carbohydrate, probably dextrose, has received the support of Benedict, Osterberg and Neuwirth;[2] these writers believe that there is normally present in urine a detectable and measurable quantity of glucose which does not reduce the copper solutions generally employed. This substance can be increased by feeding carbohydrate, and to this condition they have given the name "glycuresis." Additional evidence is furnished by Blatherwick, Bell, Hill and Long;[3] Malmros[4] says "Even though it has not been possible to produce a chemical analytically perfectly valid proof, the investigations still indicate that glucose occurs in normal urine." On the other hand Folin and Berglund[5] believe that the carbohydrate occurring in normal urine is not glucose, but a substance derived from nuts, fruits, grains and the decomposition products of foods caused by cooking. Greenwald, Gross and Samet,[6] Shaffer and Hartman,[7] Eagle,[8] and others are of the opinion that the reducing substance is not glucose, and as such, does not occur in normal human urine. As yet the controversy cannot be said to have been definitely settled; the weight of evidence seems to be that glucose, per se, does not occur in normal urine. The carbohydrate under discussion, whatever it is, does not interfere with the determination of glucose, present in pathological amounts, which is easily detectable because it produces certain definite changes in the color and transparency of the various copper solutions in general use.

It is common knowledge that other sugars and substances than glucose will give positive reduction tests. Among these are lactose, maltose, pentose, and levulose. These can be dif-

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ferentiated from glucose by employing the fermentation test, phenylhydrazin test, the use of the polariscope, and other chemical reactions, viz., Rubner's test and mucic acid test, in differentiating lactose; the Bial test for differentiating pentose; and Seliwanoff's test for differentiating levulose. There is a sufficient difference in the reactions of the various sugars to these procedures to make their differentiation possible. Such substances as uric acid and creatinin occurring in concentrated urines will at times produce a typical reduction of the various copper solutions. These can be easily differentiated by diluting the urine and further testing. Chloroform when used as a preservative may give a positive reduction test. The conjugated glycuronates which occur after the administration of certain drugs—chloral, turpentine, camphor, menthol and phenol—may be confused with glucose. The reduction produced by these substances is not the typical reaction observed when glucose is present. The glycuronates do not ferment with yeast and do not form osazone crystals with phenylhydrazin. Glucose produces a typical reduction with Benedict's solution or Nylander's reagent; it readily ferments with yeast, is dextrorotary and forms characteristic osazone crystals with phenylhydrazin.

Having determined that the reducing substance is glucose one may ask: What is the nature of the disturbance causing its presence? Is the fault primarily renal or is it a manifestation of some metabolic disorder? To determine this we have several procedures which are of value in clarifying the situation. 1. Testing each specimen of urine voided during the twenty-four hours to determine whether sugar is constantly or intermittently excreted. 2. Determining the blood sugar level after a night's fast and again two hours after the ingestion of a meal containing an ordinary helping of sugar, bread, potatoes, and dessert. 3. Utilization of the glucose tolerance test which consists of simultaneous observation at frequent intervals of the blood sugar level and urinary sugar content, following the ingestion of a definite amount of glucose dissolved in water. Before using this test it is of importance to know that the patient has not been, for any length of time, on a restricted carbohydrate diet. It has been demonstrated many times that a normal individual subsisting on a diet low in carbohydrate, when subjected to a sugar tolerance test, will respond with a marked and prolonged hyperglycemia and glycosuria which would not occur had the previous diet contained the average carbohydrate ordinarily consumed. According to the results obtained from these observations it will be possible to classify the individual as belonging to one of the following groups:

I. Renal Glycosuria: This condition is characterized by the constant presence of glucose in the urine. The sugar is excreted with a blood sugar level which is normal or subnormal. The renal threshold is low and it is supposed that the kidney is unable to prevent the excretion of sugar, which is probably a congenital or hereditary anomaly. Patients with this condition store, utilize and metabolize glucose in a perfectly normal manner; the blood sugar response to the administration

of glucose does not exceed the normal level; the patient is free from all symptoms of diabetes mellitus and when observed over a long period of time does not develop this disease.

constant presence of sugar in detectable and measurable amounts in the urine.

II. Cyclic Renal Glycosuria, Alimentary Glycosuria, or Alimentary

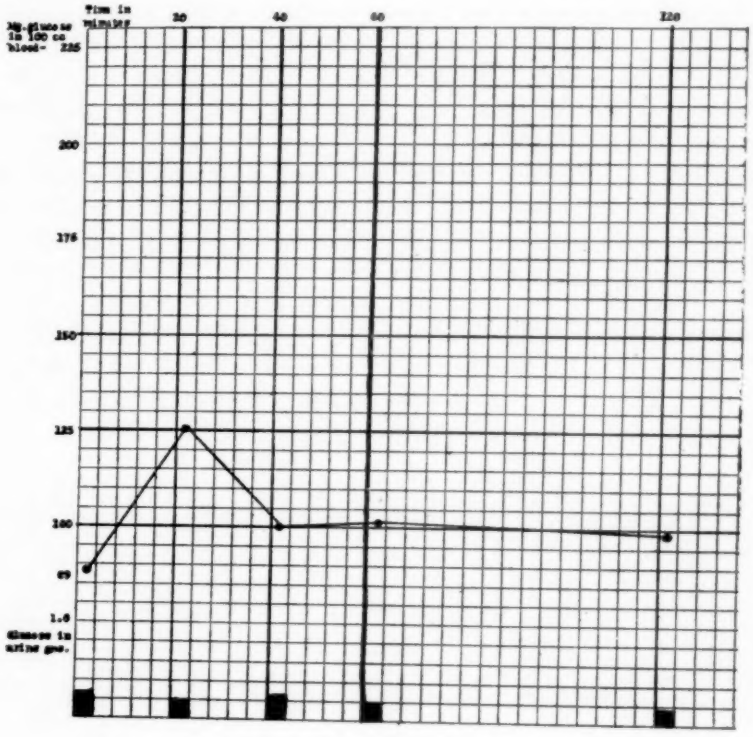

Chart I

Chart I graphically represents the behavior of the blood sugar and urinary sugar after the administration of 100 grams of glucose to a patient with renal diabetes. It is observed from this chart that the fasting blood sugar is at a normal or slightly subnormal level. Twenty minutes after the ingestion of 100 grams of glucose the blood sugar reaches its maximum level of 125. There is then a rapid decline within forty minutes to a level of 100 or it fluctuates slightly. There is a

Hyperglycemia: By these terms one understands that an otherwise normal, healthy individual excretes urinary sugar in detectable and measurable amounts after taking foods rich in sugar or starch. The glycosuria may be due to an abnormal post-prandial hyperglycemia or to a low renal threshold. Sugar is found in the urine from one to three hours after a meal. The fasting blood sugar is normal. The majority of these patients have an hyperglycemia following a meal con-

taining the average amount of carbohydrate. As to whether these individuals are perfectly healthy is not definitely settled. Some evidence is at hand which would lead us to suppose that the alimentary hyperglycemia is probably due to insufficient insulin production, in this respect, resembling a true diabetic. After the administration of 100 gm. of glucose the blood sugar reaches its peak within forty minutes to one hour and returns to a normal or subnormal level within three hours. As the sugar concentration in the blood rises glucose appears in the urine and continues to appear until concentration in the blood returns to a lower level than that at which it was first observed. Three or four hours after a sugar tolerance test an occasional person will exhibit evidence of hypoglycemic shock. This is supposedly due to an overproduction of insulin stimulated by the hyperglycemia, the pancreas getting a late start, but when once sufficiently stimulated continues with its supply to excess. A large series of these patients have recently been investigated by Malmros,[4] who believes that they have a benign glycosuria.

Chart II represents graphically the blood sugar and urinary sugar response of such a patient to the ingestion of 100 grams of glucose. It will be observed that following the administration of glucose the blood sugar rises from the normal level within forty minutes to the upper limit of normal

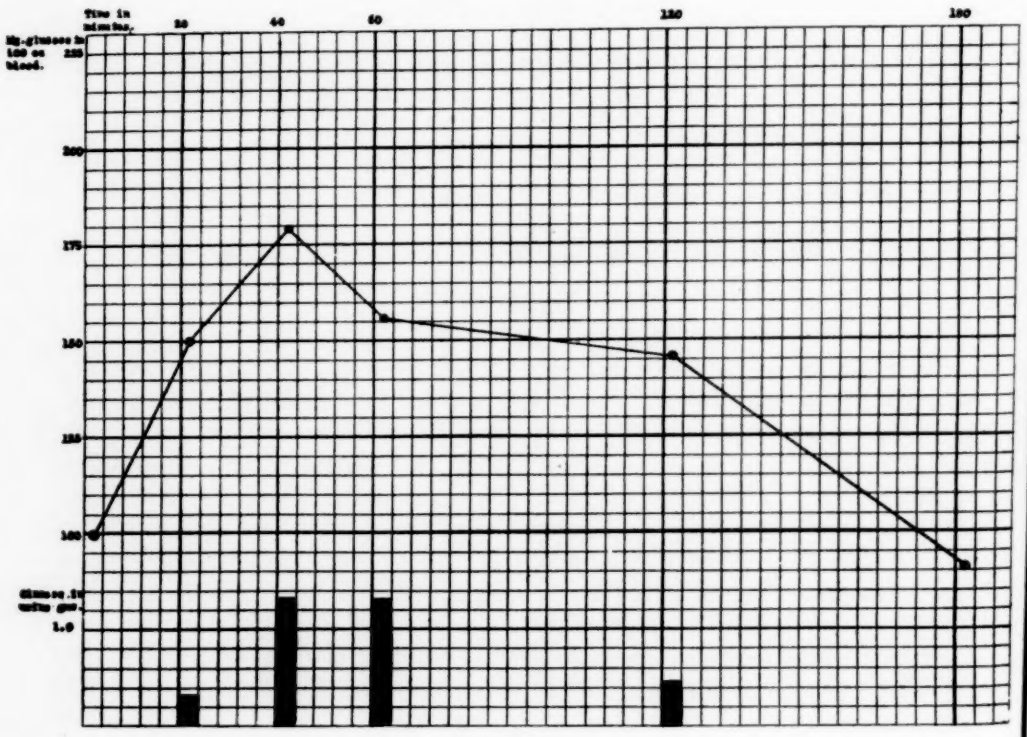

CHART II

and at the end of three hours is lower than at the beginning of the test. Sugar begins to make its appearance on the ascending side of the scale and is present in the urine with a blood sugar of 150, showing that the renal threshold in this particular patient is somewhat depressed. Sugar is present in the urine until the blood sugar level falls below 150 and at the end of three hours no sugar is observed.

III. Diabetes Innocens: This name has been given to an unusual clinical condition which shows certain characteristics of diabetes mellitus and renal glycosuria. It apparently runs a harmless course. In patients with this condition the fasting blood sugar level is normal or subnormal. There is a post-prandial hyperglycemia. The renal threshold is low, resembling that observed in renal glycosuria. Sugar is constantly excreted in the urine and there is an increase in glycosuria with an increased carbohydrate intake, but the increase is not commensurate with the increase in food. There are no symptoms of diabetes and a few patients observed over a period of years have so far not developed a symptomatic diabetes mellitus. There is no disturbance in the ability of the patient to metabolize, store and utilize glucose (Parsons).[9] After a glucose tolerance test the blood sugar rises from the normal fasting level, within an hour, to a height resembling that observed in a diabetic. The normal fasting level

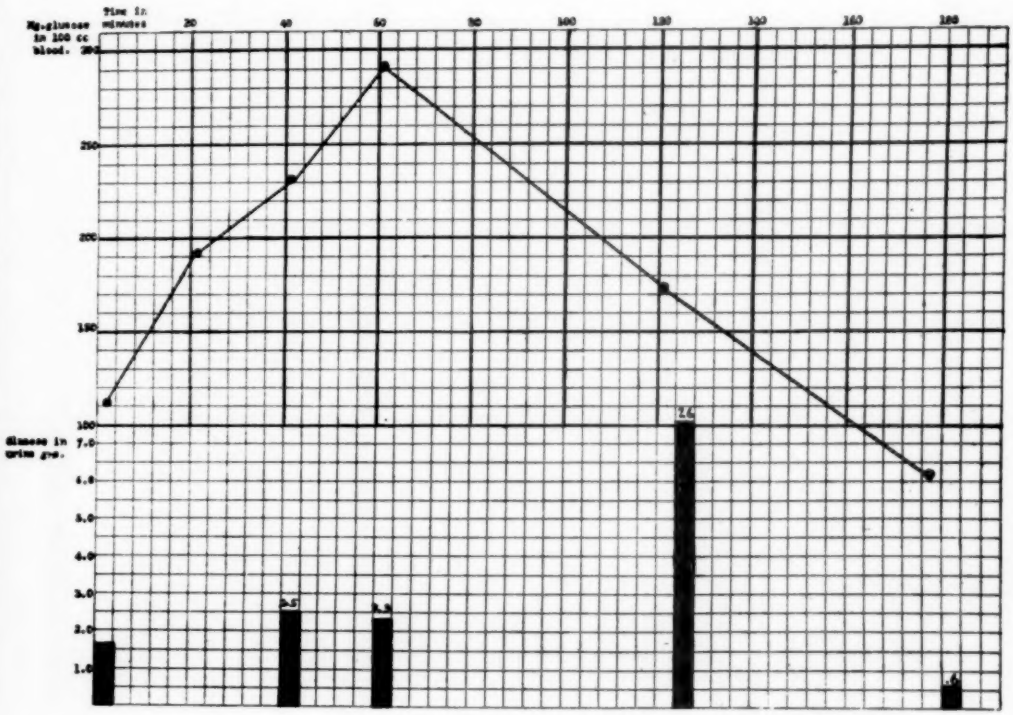

CHART III

is not reached until three hours after the administration of glucose. Sugar is constantly excreted in the urine.

Chart III graphically records the events in a patient with diabetes innocens following the administration of 100 grams of dextrose. It is observed that after one hour the blood sugar has reached a level of 290 mgms; at the end of two hours it is 175 mgms; at the end of three hours it is 75 mgms. During this entire time sugar is excreted in the urine in considerable amounts.

IV. Diabetes Mellitus: In this disease the patient is unable to mobilize, utilize or metabolize glucose in a normal manner. Experimental and clinical evidence leads us to believe that the causative factor is either a deficient insulin production or the production of an inferior quality. In the untreated cases the fasting blood sugar is above normal, rarely will one find a mild diabetic with a normal blood sugar. Glucose, as a rule, is constantly present in the urine and is greatest two or three hours after a meal containing carbohydrates; coincident with the glycosuria there is hyperglycemia. The renal threshold is normal or elevated. Because of the inability to properly metabolize glucose acidosis frequently develops.

This chart represents graphically the series of events occurring in a mild

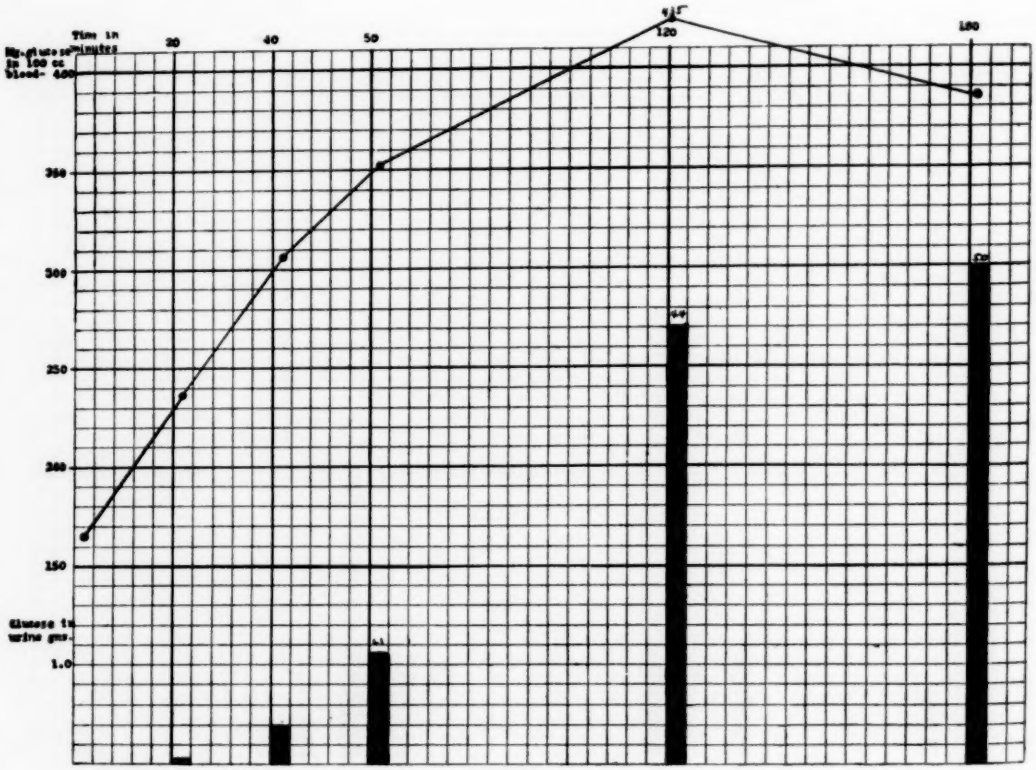

Chart IV

diabetic who was given 50 grams of glucose. It is observed that the fasting blood sugar is increased but there is no sugar in the urine voided at this time. The renal threshold is normal, or slightly increased, in this patient. The blood sugar at the end of two hours is 435 mgms. per 100 cc. At the end of three hours it is 385 mgms. There is a constant, steady increase in the amount of sugar voided in the urine.

Having determined, by using the methods outlined, to which group the individual belongs, appropriate treatment can be instituted.

REFERENCES

Baish, K.: Zeit. f. Physiol. Chem., 1895, 20, 248.

[2]Benedict, S. R., Osterberg, E. and Neuwirth, I.: Jour. Biol. Chem., 1918, 34, 217; Jour. Biol. Chem., 1923, 55, 769.

[3]Blatherwick, N. R., Bell, M., Hill, E. and Long, M. L.: Jour. Biol. Chem., 1925, 66, 801.

[4]Malmros, H.: Acta Med. Scan., 1928, Supplement 27.

[5]Folin, O., and Berglund, H.: Jour. Biol. Chem., 1922, 51, 213.

[6]Greenwald, I., Gross, J., Samet, J.: Jour. Biol. Chem., 1925, 62, 401.

[7]Shaffer, P. A., Hartmann, A. F.: Jour. Biol. Chem., 1920-21, 45, 365.

[8]Eagle, H. S.: Jour. Biol. Chem., 1926-27, 71, 481.

[9]Parsons, E.: Boston Med. and Surg. Jour., 1926, 195, p. 660.

A Surgeon's Views of the Treatment of Peptic Ulcer*

By David Cheever, M.D., *Boston, Massachusetts*

No man and no method have any monopoly of the successful treatment of peptic ulcer and in proof of this I am going to show this patient, Bennie Wean, who must be regarded as illustrating the unsuccessful treatment of ulcer by both medical and surgical means. The patient first came under observation on December 6, 1927. He is a Russian Jew, an upholsterer by trade, thirty years of age, and is married and has two children living and well. His family and previous history are both negative except for two attacks of tonsillitis fifteen years ago. His habits are good—he drinks not at all and smokes but little. He is constantly worried about his inability to earn a good living on account of his illness. This began about five years ago with a gnawing epigastric pain occurring an hour or two after eating and lasting but a few minutes. Later this became more constant and he discovered himself that it was relieved by taking food and also by taking soda which was advised by friends. After a year of varying degrees of misery he consulted a physician and was sent to an excellent hospital in Chicago (where he then lived) where he remained for seven weeks under appropriate treatment for peptic ulcer. He was discharged relieved on a modified ulcer diet of milk, cream and farinaceous food, gradually returning to more normal diet. He followed this program with considerable faithfulness but found that on every relaxation his symptoms would recur. He never vomited or noticed blood in the stools. About December 1, 1927, the symptoms had become so much worse that he applied to the Brigham Hospital for help. Physical examinination showed no deviation from the normal except for a point of moderate tenderness in the right upper quadrant close to the costal margin. Both tonsils and teeth were in excellent condition. The blood and urine were perfectly normal. Stools showed a benzidine reaction for blood. Gastric analysis showed no stasis, but hyperacidity, the free acid being 90 and the total acid 108. Barium gastrointestinal studies showed a normal stomach with no six-hour residue, a constant irregularity of the duodenal cap and a normal intestinal tract. A very small diverticulum at about the junction of the middle and the lower third of the oesophagus was noted, probably due to traction on the gullet at that point by a mediastinal adhesion due probably to an old mediastinitis. He was given careful dietetic and alka-

*Clinic before the American College of Physicians at the Peter Bent Brigham Hospital, Boston, April 11, 1929.

line treatment on the medical service for a little more than a month with considerable relief but curiously enough when enough alkaline powders were given to control his acidity his gastric motility was interfered with and there was definite evidence of hypersecretion. Although his acute pain was improved he continued to have soreness and discomfort. My colleagues felt that medical treatment at home would be even less satisfactory and that he should be offered a surgical operation, in which opinion I concurred.

Operation was done on January 6, 1928, under ether anaesthesia. The stomach was normal, the pylorus patulous. All the other viscera including the appendix were normal. Just beyond the pylorus the duodenum showed a characteristic puckered, stippled and slightly thickened area. It was determined to resect the pylorus and as much of the first part of the duodenum including the ulcer as possible. The antrum of the stomach was divided just distal to the incisura, the dissection carried down behind the first part of the duodenum and the bowel sectioned as far distal as possible, still leaving room enough to turn the end in. This dissection was carried through adhesions between the duodenum and pancreas which indicated that the ulcer was posterior and somewhat penetrating. A direct anastomosis of the open end of the stomach to the jejunum behind the colon was made with cat gut sutures. Recovery was uneventful. Pathological examination showed that the section of the bowel had passed through the edge of a practically healed ulcer. It seemed clear, therefore, that the treatment had caused at least a temporary healing of the ulcer and that the latter had been completely removed or if not that at least any remaining ulceration was entirely excluded from the gastric contents. X-ray studies on discharge showed that the barium passed rapidly through the stoma.

The patient was at first completely relieved of his symptoms but some months later developed distress without relation to meals but always relieved by powders. Nearly eight months after the operation he had several tarry stools and felt weak, and was readmitted to the hospital on the medical service on August 24, 1928. On this occasion he showed no anemia in spite of the hemorrhage. More x-ray studies showed a rapid emptying of the stomach without visible peristalsis, no six-hour residue and no demonstrable tenderness, spasm or craters. It was reported as showing no evidence of ulcer.

On this occasion he was kept nearly two months in the hospital under medical treatment. The stools, at intervals, showed traces of blood but on the whole he improved symptomatically and was discharged on October 16, 1928, with a red cell count of 5,840,000 and hemoglobin of 90%.

The third admission to the medical service occurred two months later because although the patient had been pretty comfortable during the interval he had several large tarry stools and a serious attack of weakness. On this occasion his blood showed a moderate secondary anemia but again both general physical and x-ray examinations showed no evidence of ulcer. Needless to say a search for some other

bleeding point in the alimentary tract was conducted with great thoroughness but was negative. The question of the possible responsibility of the little diverticulum of the esophagus was constantly in the minds of his advisers but it was not considered important for the reason that he had no symptoms referable to the lesion and never vomited blood. I saw him in consultation on this occasion and was encouraged by my colleagues to consider the performance of a subtotal gastrectomy but in the utter absence of evidence of any lesion of the stomach, or indeed elsewhere, I was unwilling to operate. The patient remained in the hospital for about six weeks and was discharged relieved. His fourth admission was to the medical service less than one month afterward and was the result of another much more severe hemorrhage from the bowel with marked faintness and pronounced secondary anemia; the red count getting as low as 2,000,000 and hemoglobin 30%. Now, more than six weeks after this admission he is still in the hospital. It has been slow work on this occasion to build up his blood. yesterday we made another barium x-ray examination which showed a perfectly normal stomach, emptying promptly into the distal loop of the jejunum. A little of the barium passes into the proximal loop but does not tend to pass backward into the duodenum. No crater can be made out and no tenderness to pressure. The normal rugae of the stomach can be beautifully demonstrated under the fluoroscope passing down to the point of anastomosis without modification of their arrangement. There is not the slightest evidence of ulcer. Gastric analysis shows a fair acidity on the fasting contents and a maximum acidity on the withdrawal of the fourth specimen of 55 free acid and 72 total acid.

Now, what are we to think of this patient? It seems fair to say that medical treatment has been a total failure. No doubt if the patient could have given up any form of activity and remained hospitalized and fed on slops and powders he could have been kept fairly comfortable and possibly the hemorrhages would have been averted, but it is hardly reasonable to expect that a patient should submit to such treatment continuously for sixteen months. The patient states on close questioning that since the operation of January 6, 1928, he has been free from the old ulcer pain which was so severe and that the discomfort which he usually complains of now is of a different sort, situated in a different place and is not very severe. He feels that if it were not for the hemorrhages he would be able to carry on his vocation and would be well satisfied. It may be said, therefore, that the operation has to a considerable degree relieved symptoms and has somewhat reduced the acidity but the hemorrhages which jeopardize his life certainly make it necessary for us to adjudge the surgical treatment also as a failure.

Let me leave Bennie Wean for a moment and discuss certain general impressions which have been crystalised in my mind during the years in which I have been trying to accomplish something with peptic ulcer. As to the etiology of the condition my

impressions are chiefly of a negative sort. Many, but not all, of these patients are of "nervous" or high-strung temperament; many, but not all, among the men, are excessive cigarette smokers; many, but not all, carry burdens of worry or anxiety; many, but not all, have bad teeth and some have infected tonsils. In every patient upon whom I have operated I have made it a point when possible to examine all the abdominal viscera and usually to remove the appendix. I have never observed the incidence of appendicular lesions with any more frequency than would have been the case in an equal number of abdominal sections made for other purposes. I have not noted any association with cholecystitis and therefore I cannot consider the theory of focal infection from these sources at all seriously. The theory of emboli of the arterioles of the stomach and duodenum with resulting necrosis and digestion of tissues has not impressed me, for I cannot see why these patients who are so often young and otherwise healthy should have emboli in this particular locality and never show evidences of emboli elsewhere. It is quite true that small emboli in most organs might be without symptoms but certainly they should sometimes strike in places where the symptoms would be equally or more serious than in the case of the upper alimentary tract. The one striking fact which has always been emphasized in ulcer cannot be excluded, namely, that the overwhelming majority of ulcers occurred in a limited area along the lesser curvature of the stomach, antrum and the first portion of the duodenum and that this area is precisely where traumatism is most likely and where hyperacidity is greatest. The partially masticated food when ingested lies at first in the proximal and middle portions of the stomach rather inertly and for a considerable time retains its alkalinity derived from the saliva. It is true that the acid secretion is derived chiefly from the glands in the pars media of the stomach rather than in the antrum but the acidified chyme is gradually pushed down into the antrum where it is subjected to the extremely vigorous churning peristalsis of that portion of the viscus. It seems reasonable to believe that a combination of vigorous muscular action and poorly masticated food may result in trauma to the mucosa—a trauma which at once leads to auto-digestion by the strongly proteolytic acid gastric juice; the same is true of the first portion of the duodenum where chyme of the same character is pounded by the action of the sphincter and the vigorous peristalsis of the first part of the duodenum. Once the chyme passes from the first into the second portion of the duodenum its acidity is neutralized by the bile and pancreatic juice and by the same token we cease to meet (with negligible exceptions) with spontaneous ulceration.

Naturally, other factors almost too numerous to mention enter in. If a patient has abscessed teeth and a foul mouth it is likely that the food is but little masticated and more likely to cause trauma. If he is worried and anxious and depressed over his inability to pursue his vocation and earn a proper living for his family it is likely that his gastric glands will be stimulated to increased secretion. Beau-

mont's observations more than one hundred years ago of the influence of the emotions on the gastric secretions as observed through the fistula of Alexis St. Martin are as sound now as when they were first reported. Once an ulcer has formed at or just beyond the pylorus its irritation causes pylorospasm, retention and therefore increased secretion. Perhaps this influence is exerted by those legendary messengers "Hormones."

We are justified in conceiving of frequent minor traumatisms of the mucosa with slight auto-digestion of the devitalized tissue causing slight erosions which result in heart burn and discomfort but are promptly and completely repaired by the healing processes. In a certain instance, however, the traumatism may be more severe, the auto-digestion more intense, and the struggle between the proteolytic and reparative processes waxes and wanes with success attending first one and then the other until finally chronic inflammatory changes take place in the wall of the viscus at the disputed point with increasing fibrosis, contraction of the tissues about the arterioles and consequent starvation of the ulcer, rendering it relatively devitalized and more easily attacked by digestive ferments. Thus is formed the chronic indurated peptic ulcer.

Medical treatment which aims to correct hypersecretion by rest and diet, to relax pylorospasm, and to neutralize the acid by chemical means is logical and rational. That it usually secures permanent healing in early cases is undoubted; that it relieves symptoms if it can be consistently pursued is certain; but in the case of the chronic indurated ulcer how often does it cure in the sense of restoring the patient to a condition where he is not more liable to a recurrence of ulcer than is a normal individual to develop the lesion de novo? Very seldom, according to my belief. As I have observed my friends who have been successfully treated for ulcer, by medical methods, they appear to me to have one eye on their diet and another on the bicarbonate of soda bottle, and to be usually trying to avoid fatigue. They seem to be rarely more than two jumps ahead of the ulcer! And this is the situation among those who can afford to live at a reduced level of activity and to take care of themselves. Can the average patient, as we meet him in hospital and office practice, afford to pay to his ulcer the tribute demanded in terms of enforced inactivity, special diet and medicine with all the disadvantages which these measures entail? No doubt some patients may be symptomatically cured of their chronic ulcers by a careful course of medical treatment but I personally believe this to be uncommon. Much more common is the patient who can be set on the right track by medical regime and may then keep himself comfortable by habitual selection and limitation of diet, by diminishing his vocational and other activities, by enforced rest and occasional alkaline medication. All too common is the large group where the price paid for reasonable comfort is eternal vigilance, habitual renunciation of both wholesome work and of many pleasures, strict diet and constant medication. The average man has not the means or self-control to carry out these measures; therefore,

he muddles along between periods of physical misery with nervous depression and of comparative well-being bought at the price of self-denial and inactivity which may bring his family face to face with want, and a certain small percentage of these patients will die of acute perforation or hemorrhage unless saved by an emergency operation.

Surgery proposes a method of treatment as rational and logical as that offered by medicine, and based on the same underlying principles though accomplished by mechanical measures. It can remove the ulcer or segregate it from the acid gastric contents; it can do away with pylorospasm and secure more rapid emptying of the stomach, hoping thus to diminish hypersecretion and hyperacidity; it can do away with obstructing cicatrices which interfere with motility. The price it exacts is a small operative mortality and the discomforts and complications attending operations in general. Its results (excluding the fatalities and certain rare complications) at their worst are no more evil than failures in medical treatment. At their best they are superior, on the whole, to the results of the medical management of obstinate chronic cases which are the only ones (barring the acute perforations) which should be operated on. It is the misfortune of surgery that its failures excite more criticism and disparagement than those of medicine because of the ordeal to which the patient is submitted,—an ordeal, by the way, which is often much exaggerated.

Let us review briefly the types of procedure and of the advantages and disadvantages which they offer, considering first duodenal ulcer which is by far the most common form. Gastro-jejunostomy is the simplest and safest procedure. If it succeeds in diverting the whole of the acid chyme from passing through the pylorus and in causing a prompt emptying of the stomach, it secures the two great desiderata—segregation of the ulcer and diminution of secretion and is likely to give a brilliantly successful result. Unfortunately there can be no assurance that the new stoma will function perfectly; almost always if the pylorus is patent some of the chyme will pass through this normal channel and attack the ulcer, and secretion will not necessarily be diminished. Moreover, the point of union of stomach with jejunum may offer a point of diminished resistance where a new ulcer may form. In spite of these disadvantages gastro-jejunostomy is the most practised procedure and gives many excellent results.

Resection of the ulcer with a simple plastic operation on the pylorus after the Heineke-Mikulicz plan is feasible only if the ulcer is situated anteriorly and is likely to be unsatisfactory because it appears that secondary contraction of the scar is apt again to narrow the pylorus and cause retention and hypersecretion. A more elaborate type of pyloroplasty by the Finney method is more likely to succeed, though, here again, if the ulcer is to be excised we are limited to those situated anteriorly and in some cases also restoration of pyloric function and spasm may occur. Nevertheless this method in our hands has given some brilliant results.

Exclusion of the pylorus by some form of plication or ligation, with gastro-jejunostomy, rarely succeeds since the lumen usualy restores itself. Complete exclusion of the ulcer, or better still its extirpation, with some measure to promote rapid emptying of the stomach, seem to me to offer the most logical plan and in this opinion I am supported by an indication given by Nature herself, for it is widely admitted that a duodenal ulcer which has resulted in cicatricial closure of the pylorus is most favorable for permanent cure by gastro-enterostomy. Why may we not imitate this by surgical exclusion? The pyloric antrum is transected vertically at the incisura, the dissection is carried behind the pylorus and first portion of the duodenum as far as possible and the bowel divided beyond the ulcer. A direct anastomosis may then be made, if the structures are mobile enough, between the open end of the stomach and the duodenum,—a method frequently called the Billroth No. 1. Thus it is assured that the gastric contents will be propelled by the normal peristalsis in its accustomed course and the absence of the pyloric sphincter mechanism should promote rapid emptying of the stomach. If the direct anastomosis to the duodenum is not feasible, the stomach may be anastomosed to the jejunum either by its already open end (Polya) or by closing the opened end and making a posterior gastro-jejunostomy, which I believe to be the preferable method. If, as frequently happens, the penetration of the posteriorly situated ulcer into the substance of the pancreas makes it impossible to resect the duodenum, the divided antrum is closed by suture, which, of course, effectively segregates the ulcer from the acid chyme, and the operation is completed as before. It is my present belief that a completely excluded ulcer will almost invariably heal. This method appears to have given many most satisfactory results. I have not been able to approve of the subtotal gastrectomy for duodenal ulcer, as in spite of favorable statistics I believe that it is likely to entail an excessive mortality and also that it is undesirable to impair so seriously the useful, if not absolutely essential, function of the stomach.

How shall we select the operative procedure to be used? I believe that the resection or total exclusion type of operation should be considered the ideal and should be employed if possible, but if the local conditions found make it too difficult technically to carry out with comparative safety, it should be abandoned and a simpler operation, usually a gastro-jejunostomy, carried out. If the patient is very adipose or in any other way an unfavorable subject, gastro-jejunostomy should be the operation of choice and in experienced hands ought to be almost free from mortality. We must be content to do something less than the theoretically ideal inasmuch as we are not dealing with a progressively fatal disease but one in which the operation may usually be considered highly expedient rather than absolutely necessary.

Turning for a moment from duodenal to the far less common gastric ulcer the same general principles may be said to apply. Resection of the ulcer with gastro-jejunostomy to promote rapid emptying of the stomach is

the operation of choice but often the ulcer is so situated or so extensive that the surgeon will be forced to carry out a more extensive attack with resection of a considerable portion of the stomach and appropriate restoration of gastro-intestinal continuity, very likely by ante-colic direct anastomosis of the jejunum of the Polya type. Here, again, if difficulties are encountered or the patient is not a good subject, the surgeon should be content merely with a gastro-enterostomy, for I am very decidedly not one of those who believes that a primary peptic ulcer is often the starting point of carcinoma.

It is hardly necessary to amplify what I have said in defining my attitude toward ulcer by emphasizing what all physicians and surgeons alike are agreed on, namely, that acute perforation, persistent recurring bleeding and cicatricial contractions causing serious motor disturbances require surgical measures for their attempted relief.

Let us now return to this patient, Wean,—he is the first who has apparently completely disproved my contention that a completely excluded ulcer will heal, but since we can find no other source of his hemorrhage, even though the ulcer has been nearly completely resected and excluded, we must assume that the bleeding is from the same source. He presents indeed a serious problem. It is clear that we cannot conscientiously trust or hope that these hemorrhages will now stop spontaneously. We must explore and I have the impression that our examination of the stomach, the anastomosis and the afferent and efferent limbs of the jejunum will fail to show externally any evidence of a new ulcer. We must then examine the duodenal stump, and, buried as it is in scar tissue, underneath the liver and in relation to the bile ducts and head of the panceras, I doubt very much whether we can get by inspection or palpation any reliable evidence of ulcer. Nevertheless, I shall be in favor of freely opening the duodenum in order to make absolutely certain of the condition. If an ulcer is found, it will probably lie directly upon the gastro-duodenal artery or one of its main branches in relation to the head of the panceras. I think the further procedure will present a serious problem but I hope that it may be possible to excise still more of the duodenum, with or without ligation of the artery. The trouble is, of course, that the anastomoses of this vessel with pancreatic or duodenal branches from a different source—the superior mesenteric—are so free that we cannot expect too much from ligation of a single trunk. I should feel at any rate that the only possible effort will have been made to repair a lesion which is likely to be fatal if something cannot be accomplished.

Let me show you for a moment this other patient, Abraham Fine, who represents about what I have learned to expect as the immediate result of these operations. He is also a young Russian Hebrew who developed ulcer symptoms about two years ago, was diagnosed and treated medically first in the wards and then in the excellent special clinic of the Massachusetts General Hospital, obtained only partial relief and was finally advised to have an operation, which at the time he

refused. His misery continued, he was unable to work, his anxiety about his wife and family became acute and when he fell into my hands he was anxious to accept the possibility of operative relief. X-ray showed a typical duodenal deformity with slight gastric stasis. At operation the antrum was divided, resection found impossible on account of penetration into the pancreas, the ulcer completely excluded by closure of the antrum and a posterior gastro-jejunostomy made. Here he is now completely free of symptoms, and rapidly regaining his strength. He states that from the moment he recovered sufficiently from the anesthetic to analyze his feelings he has not experienced a moment of the old ulcer pain. He is on a six-meal diet of milk, cream, cereals, toasted bread, eggs, orange juice and occasionally a little chicken. Barium x-ray studies made yesterday show that there is no residue, the ingesta passing rapidly down through a satisfactory stoma into the distal loop. Gastric analysis has not been made but there is very good reason to believe that secretion has been much diminished. Were it not for the case of Bennie Wean I would say with much confidence that the excluded ulcer will heal and remain permanently out of the picture. In spite of this disappointment I think that Abraham Fine, if he takes reasonable care of himself, can lead, without discomfort, an active and useful life and support his family.

It would be easy to pack the floor of this amphitheatre with old patients illustrating the successful surgical treatment of ulcer but I think it would add nothing to this demonstration because you and I both know that it could be packed also with the unsuccessful examples of surgery and with the successes and failures of medical treatment. I have intended to be, and I hope that I have given you the impression of being entirely candid in the expression of my views. The successful handling of a patient with ulcer depends not upon rigid adherence to one viewpoint but on willingness to recognize the usefulness of different forms of treatment and to select and apply with skill and patience that method which is best adapted to the individual patient. The best criterion of sincerity is the course chosen by the physician himself if he were afflicted. I am quite clear in my mind that if I were so unfortunate as to have a peptic ulcer I would take a prolonged vacation and put myself in the hands of my medical colleagues for careful and rigid treatment; that I would then resume reasonable activity with moderate dietary restriction and if I had another exacerbation I would repeat the process; if then, I found that I could not pursue a reasonably active and useful life and that I must submit to irksome and distasteful dietary restriction and medication for an indefinite time, I would gladly turn to any relief which surgery might offer.

The Suprarenal Glands and Hypertension:

A Study of the Veins Within the Suprarenal Glands*

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In 1855 Addison described a clinical syndrome due to disease of the suprarenal glands. In his description there is a hint of the physiologic relationship between these glands and the cardio-vascular system; for he found "the pulse, perhaps, large but remarkably soft and compressible" and "remarkable feebleness of the heart's action." In the opening paragraph of his thesis Addison said in part, "The functions of the suprarenal capsules are almost or altogether unknown" and "I am not aware that any modern authority has ventured to assign to them any special function or influence whatever."

In the seventy-three years that have passed since Addison's statement, numerous contributions on the suprarenal glands have served steadily to increase the large store of information which was so obviously absent in Addison's day. Only the most important contributions, and those pertinent to this paper, can be mentioned here. They are: (1) death follows promptly and characteristically after removal of both suprarenal glands (Brown-Séquard, 1856); (2) the aqueous extract of the medulla of the suprarenal glands has a distinct action on the blood vessels and heart, causing vasoconstriction and raising the blood pressure (Oliver and Schäfer, 1894, and Cybulski and Szymonowicz, 1895); (3) there is a similar substance in the veins of the suprarenal glands (Langlois and Cybulski and Szymonowicz, 1897, and Dreyer, 1899); (4) isolation of the actual principle (epinephrine) of the medulla of the suprarenal gland (Abel, 1899); synthetic preparation of this substance designated suprarenin (von Fürth, 1900); (5) stimulation of splanchnic nerves causes increased secretion of epinephrine (Dreyer, 1899); (6) independent isolation of the active principle of the medulla of the suprarenal gland, called "adrenalin" (Aldrich and Takamine, 1901); (7) epinephrine produces the same effect on certain structures as direct stimulation of splanchnic nerves (Lewandowsky, 1900), and (8) the confirmation of von Fürth's work (Dakin, 1905). In the early period of investigation of the function of the suprarenal glands, it was believed that epinephrine was the product of the medulla only and that the medulla was essential for life.

*Abridgement of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the degree of Master of Science in Medicine, 1928.

However, Biedl[6] and Wheeler and Vincent demonstrated that fishes and other animals could live if deprived of all the medullary tissue of the suprarenal glands. This implied that epinephrine was not essential for life but Kohn[30,31] showed a chromaffine substance like that in the medulla of the suprarenal gland, in other situations; Fulk and MacLeod presented evidence that the active principle of the retroperitoneal chromaffine system has the same physiologic action as epinephrine, and Hartman demonstrated the presence of epinephrine in the cortex of the suprarenal glands.

The value of epinephrine to the normal organism is controversial. Stewart and Rogoff showed that the spontaneous liberation of epinephrine was abolished as far as could be determined by section of both sympathetic trunks and that cats survived indefinitely the removal of one suprarenal gland and section of the nerve supply to the remaining gland. Gley maintained that epinephrine is not of physiologic significance and is probably a product of waste or excretion; Stewart believes it is a relic of some remote philogenetic epoch, that all functions of the suprarenal gland are dependent on the cortex, and hence that clinical syndromes of suprarenal insufficiency are purely inventions of clinicians of uncurbed imagination. These views are vigorously combated by Pende, who brings to his support the work of Roux and Taillander; Marshall and Davis; Hartman and Blatz; Hartman; Cannon; Cannon, Udill and Griffith, and others.

In view of the opposed opinions of these protagonists and antagonists concerning the value of epinephrine, a middle path only can safely be pursued. Two facts are obvious: the suprarenal glands are essential for life and they produce epinephrine, which is capable of provoking widespread vasoconstriction and increase in the arterial blood pressure. It has not been proved that epinephrine is necessary for the maintenance of normal vascular tone and blood pressure.

Seventy-three years of observations and investigations have not brought certain problems regarding the rôle of epinephrine in the normal organism to an acceptable conclusion. Its status in hypertension is equally chaotic, for, as Mosenthal has said, "This idea (epinephrinemia as a cause of hypertension)* has been categorically affirmed and denied." My study, which is purely one of morphology, is presented with full recognition that a physiologic interpretation on such a basis is extremely hazardous, but according to Cannon: "It is too bad that the separation of histology from physiology has become so sharp."

Morphologists have long been aware of the well developed musculature of the veins of the suprarenal gland. Attention has been called to the distribution of this musculature in masses running longitudinally to the axis of the vein, a unique arrangement when contrasted with musculature of veins elsewhere in the body. The absence of circular muscle in the central vein and tributaries has been noted. Henderson and Goldzieher and Sherman have reviewed the literature essential for an understanding of this musculature, and the former demonstrated it by actual

*Parenthesis and contents mine.

reconstruction. Without doubt, many students of pathology have noted differences in volume of the muscle masses in the veins of suprarenal glands removed at necropsy in cases of normal and high blood pressure. Robertson has observed this condition over a period of twenty years and this paper is an outgrowth of a suggestion made by him. Accurate estimations of these differences have been lacking.

Materal and Method

The tissue used for study had been removed at necropsy and preserved in solution of formalin. Many of the glands had been cut in two or more sections for routine study. All pieces of any considerable size were sectioned provided they contained one pole of the gland. No attempt was made to differentiate right and left glands. Sections were cut approximately 1, 2, 3 and 4 cm. from either end of the gland, through a line perpendicular to the convex surface. These sections were numbered 1, 2, 3 and 4 in each piece of tissue studied, depending on the distance from the pole of the gland (fig. 1).

Glands from two groups of cases were studied: those of so-called essential hypertension, and those of normal or low blood pressure. From the latter group were excluded all cases of primary cardiac disease and myocardial degeneration, nephritis, brain tumors, injuries with shock, hyperthyroidism, fever from any cause, myxedema, jaundice, emaciation or exhaustion from any cause, and hypertrophied prostate gland, as these conditions might influence the blood pressure unduly. The group included the glands from patients who had died as a result of operation for carcinoma, chronic ulcerative colitis, progressive bulbar palsy, pregnancy with hemorrhage, intestinal obstruction, chronic cholecystitis with stones and diaphragmatic hernia. The average blood pressure, in millimeters of mercury, in the hypertension group was 200 systolic and 110 diastolic; the average age was fifty-four years. The average blood pressure in the normal group was 126 systolic and 78 diastolic; the average age was forty-eight years. Sixty-eight sections from eighteen cases of known hypertension and fifty-seven sections

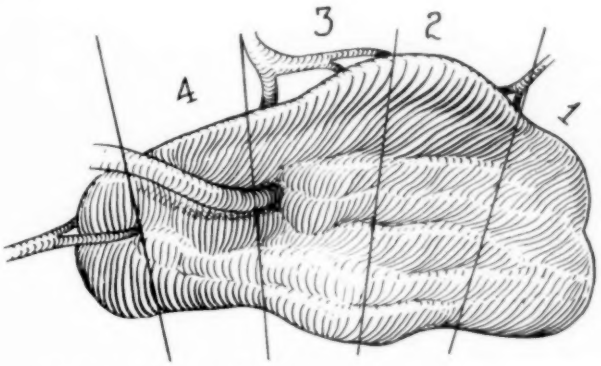

Fig. 1. The method of cutting each gland into sections.

from twenty-five cases in which the blood pressure was normal serve as the basis of this study. The tissue was imbedded in paraffin and stained by Weigert's elastic-tissue and van Gieson's connective-tissue stain. The former aids in the identification of arteries, the latter of muscle.

The problem of identifying veins and excluding arteries was immediately apparent on microscopic examination. The following standard for identification was adhered to (figs. 2 and 3):

ARTERIES

Walls of uniform thickness
Circular lumen
Circular muscle present
Longitudinal muscle regularly distributed on all sides of the vessel
Internal elastic lamina present

VEINS

Walls of greatly varying thickness
Irregularly shaped lumen
Circular muscle absent
Very irregularly distributed longitudinal muscle
Internal elastic lamina absent

Vessels with an actual maximal outside diameter of less than 0.4 mm. were not measured, and if the maximal actual thickness of the muscle of any vein was less than 0.06 mm., it was considered to be without musculature. Throughout this paper, the term "veins without muscle" applies to this group, and to those veins actually without muscle. All vessels without muscle and with diameters in excess of the minimum for measurement were considered veins, although many of them were doubtless endothelial lined sinuses connecting the arteries and veins. All veins so chosen for study were projected on ordinary white paper and drawn at magnifications varying from 25 to 200 times. These drawings were then measured with the planimeter, an instrument which provides such an excellent means of calculation in this type of work that it is surprising it has not been more extensively used. It consists essentially of a fixed mass with a pivoting arm which fits into a socket. This socket may be moved back and forth on a bar which has, at one end, a pointer with a finger grip; on the other end is a double scale by which calculation may be carried to the third decimal place (fig. 4). At the beginning of any piece of work the movable socket is fixed on the bar by a screw, thus preventing changes in the distance relationship to the scale and the pointer. The value of 1.0 on the scale must be determined. The following will illustrate how this determination is made: A primary reading of, for example, 1.165 is made, the pointer is moved around the circumference of a known area of 100 sq. cm. and a second reading of 2.365 is taken. The difference between the first and second readings constitutes the final figure, 1.2. Then the value 1.2 on the planimeter scale equals 100 sq. cm. of surface area and the value 1.0 equals 83.33 sq. cm. (1.2:1::100:x) Subsequently the absolute surface area of projected images can be determined with accuracy by multiplying the final reading on the planimeter scale by 83.33. The calculated constant will change with changing conditions. Marked irregularities in the outline of areas measured do not constitute an obstacle to accuracy if the planimeter is used.

In each vein with muscle, the area included within the maximal circum-

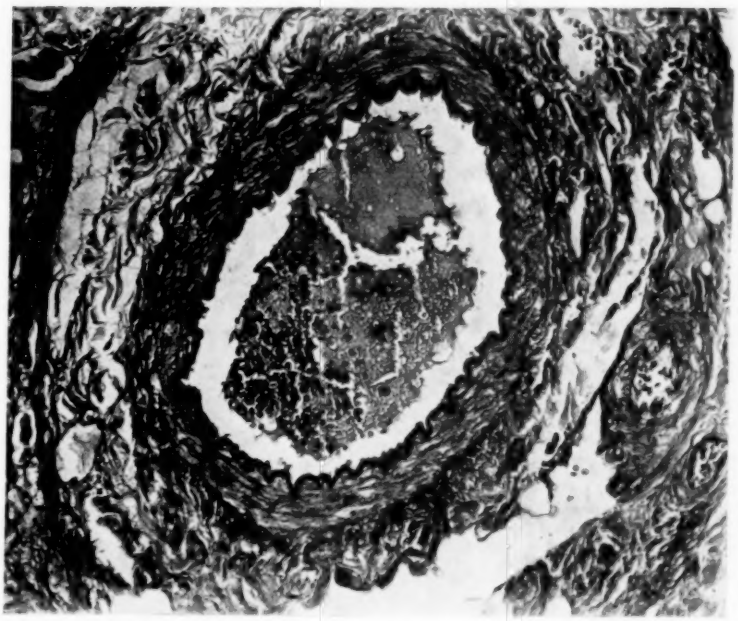

FIG. 2. Weigert stain of an artery in the substance of the suprarenal gland, showing the circular lumen, the regularly distributed muscultaure and the internal elastic lamina (X 110).

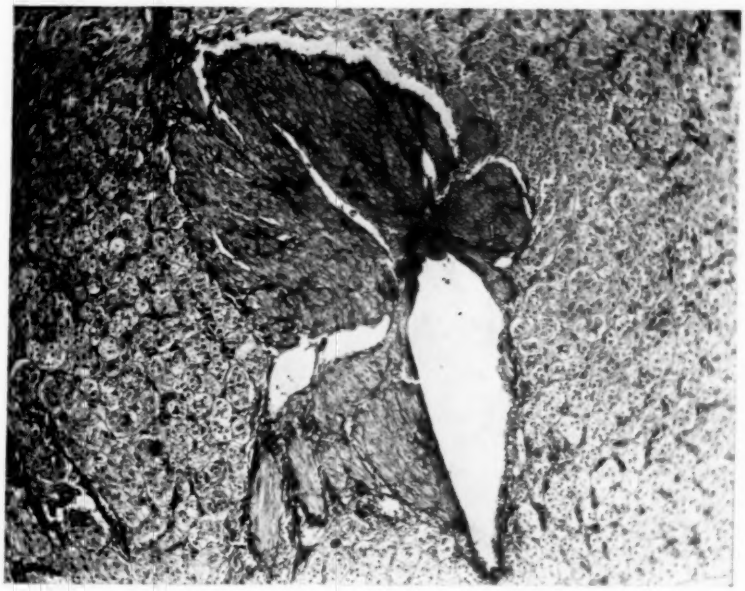

FIG. 3. Weigert stain of vein from the substance of the suprarenal gland showing the irregular lumen and longitudinal muscle masses, the absence of circular muscle fibers and internal elastic lamina (X 60).

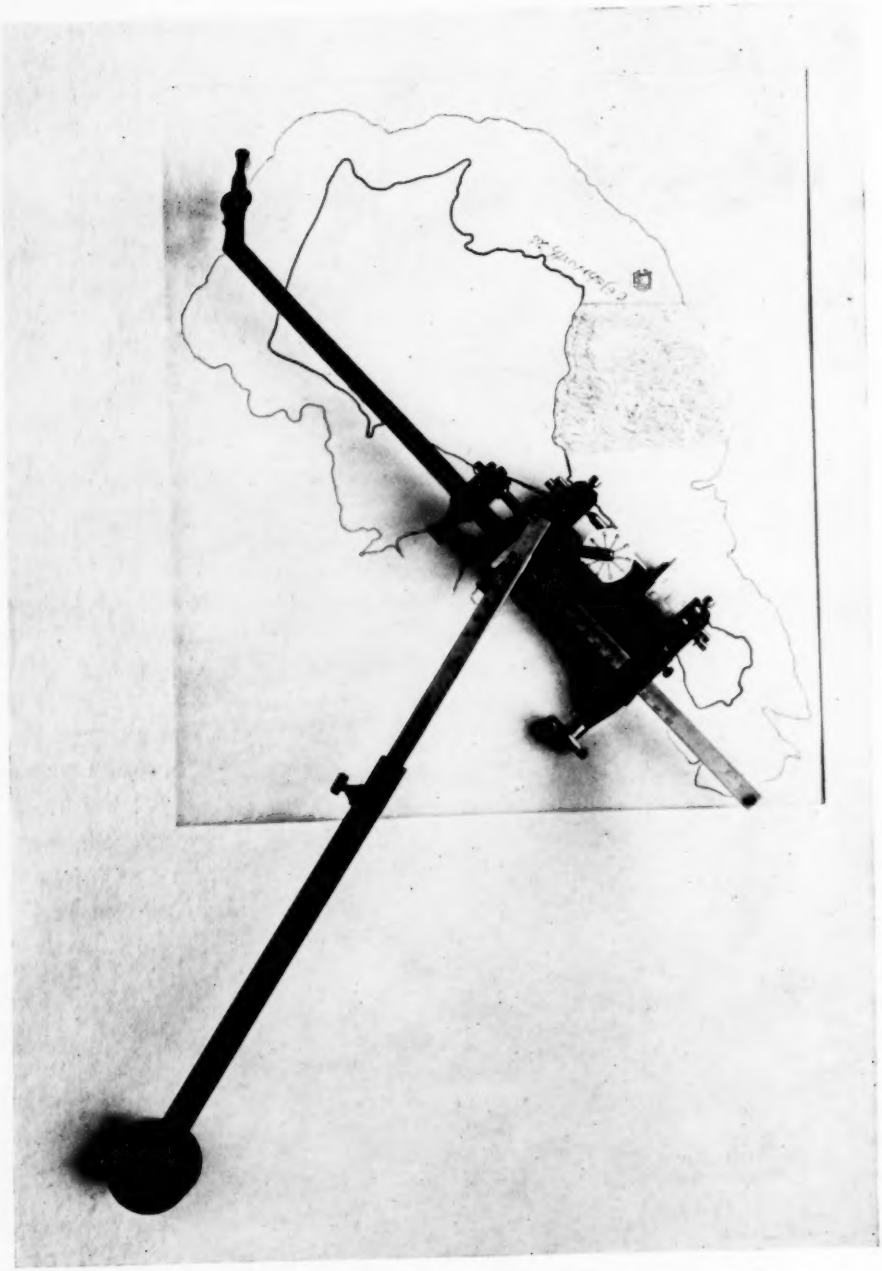

FIG. 4. The planimeter in place over a diagrammatic drawing of a vein.

ference of the vein and its muscular wall was calculated; the second estimation was of the area of the lumen; the difference between the first and second figures was considered the area of the muscle. More than 1300 such measurements were made in this study of approximately 750 veins. After the areas of the lumen and of the muscle of the projected image is known, the absolute area is determined by dividing by the magnification. The ratio of muscle to lumen of any vein is calculated by dividing the absolute area of the muscle by the absolute area of the lumen.

In order that a comparison might be made of the veins removed from the same areas in the two groups, the number 1 section of the hypertension group was compared with the number 1 section of the normal group; the number 2 section of the hypertension was compared with the number 2 section of the normal group, and so forth. For comparison of veins of equal size, they were divided into groups depending on the absolute area of their individual lumens regardless of their situation in the gland as follows:

Group 1	Less than 10 sq. mm.
Group 2	10.0 to 19.9 sq. mm., inclusive
Group 3	20.0 to 29.9 sq. mm. inclusive
Group 4	30.0 to 39.9 sq. mm. inclusive
Group 5	40.0 to 49.9 sq. mm. inclusive
Group 6	50.0 to 59.9 sq. mm. inclusive
Group 7	60.0 to 69.9 sq. mm. inclusive
Group 8	70.0 to 79.9 sq. mm. inclusive

Larger veins were grouped according to the foregoing system.

Objections to the Method

The method of estimating the ratio of musculature to lumen by measuring diameters of the lumen and thicknesses of muscle is open to much criticism. This is particularly true in measurements of the musculature and lumens of the veins of the suprarenal gland, in which the lumens and masses of muscle are extremely irregular in diameter and thickness (figs. 3, 5, 6, 7). These irregularities make the method of measuring diameters of the lumens and thicknesses of the walls inaccurate and impractical. Even in vessels in which the lumens and the distribution of muscle are regular, this method does not give information of the actual ratio of the total mass of muscle surrounding the vessel to the area of the lumen, but only the ratio of the thickness of the muscular wall to the diameter of the lumen.

The use of the planimeter obviates all error of determination of the relative sizes of lumen and musculature as represented in the projected drawings, regardless of the irregularity of the lumens or of the masses of muscle. It does not, however, influence the error in the manner of study previous to and including the drawing of the projected image of the vessel. These errors are present in all methods. Three factors interfere with absolute accuracy: (1) it is impossible to cut sections from the suprarenal gland exactly at right angles to the convex and flat surfaces; (2) the veins pursue an irregular course through the substance of the gland and are thereby cut at many angles, and (3) it is sometimes difficult, even with the van Gieson stain, to determine at what point musculature terminates and surrounding fibrous tissue begins. This is particularly true in sections in which

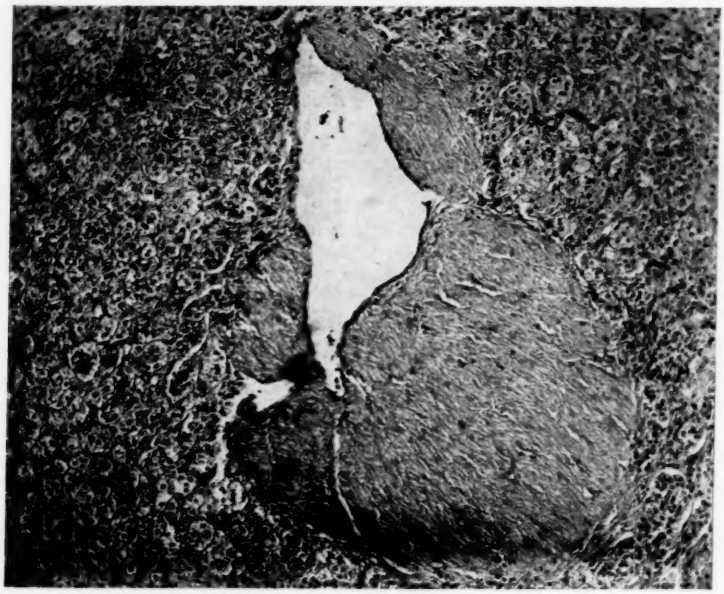

FIG. 5. Vein from a suprarenal gland in a case of hypertension, showing the enlarged longitudinal muscle masses (X 100).

FIG. 6. Vein from suprarenal gland showing marked hypertrophy of the muscularis in a case of hypertension (X 100).

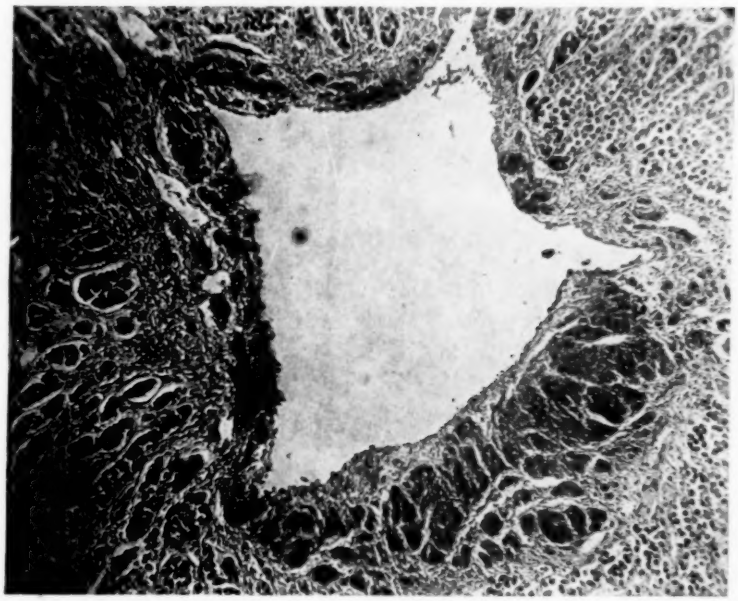

FIG. 7. A vein from a suprarenal gland in a case of normal blood pressure. The cross section area of muscle is comparatively small when compared with the cross section area of the lumen (X 75).

isolated bits of muscle are found separated from the muscle, and in those in which the fibrous tissue pushes in around the outer edge of the muscle. Since there seems no way to obviate these difficulties, they must be borne in mind, but must be considered common to both groups studied. The method of measurement with the planimeter, even with its limitations, is vastly superior to other methods for determining the relative sizes of vessels and their walls.

RESULTS

The muscle-lumen ratio: The ratio of muscle to lumen of veins of the suprarenal glands in cases of hypertension can be accurately compared with the ratio of muscle to lumen in cases of normal blood pressure only if vessels of comparable size are studied. For this purpose, all veins with musculature were grouped according to the area of the lumens, as described. Veins, of the suprarenal gland in which the individual actual area of the lumens is in excess of 29.9 sq. mm., are rare in cases in which the blood pressure is normal, and for the purpose of comparison of the ratio of muscle to lumen in the hypertension and the normal groups, all veins with a lumen area in excess of 29.9 were considered in group 4. The results of this study are shown in table 1 and figure 8. As the lumens increased in size in the veins of patients whose blood pressure was normal the total mass of muscle relatively decreased. The veins of the patients with hypertension, with areas of lumen less than 20.0 sq. mm. showed the

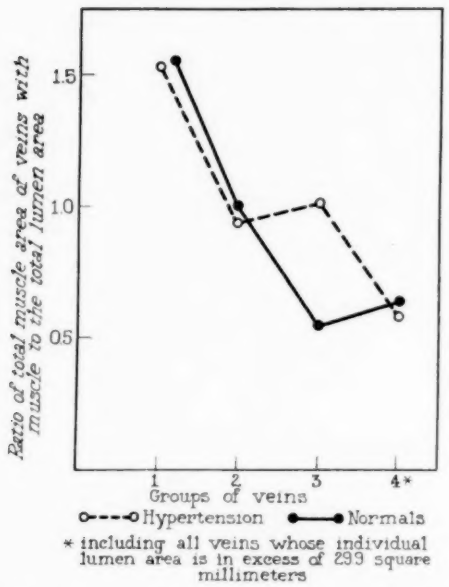

FIG. 8. Comparison of the ratio of muscle to lumen in cases of normal and high blood pressure. This ratio as compared with the normal is approximately twice as great in veins of group 3 in cases of hypertension. In the ratios, which are expressed as single values, the unexpressed quantity is understood to be 1. That is, the highest ratio would read 1.5 to 1.

same decreasing proportion as the veins become larger. Hypertension veins of group 3, however, deviated markedly from the normal, and instead of the amount of muscle in proportion to the lumen decreasing, it actually increased (figs. 5 and 6). Whereas, in the group 1 veins, the 1.5* ratio of hypertension veins compared favorably with 1.5 ratio in normal veins and the 0.87 ratio of the hypertension veins of group 2 compared favorably with the 0.97 ratio of the normal veins; the 0.99 ratio of the hypertension veins of group 3 was almost double the 0.57 ratio of muscle to lumen in the normal veins. This is excellent evidence that the hypertension veins of group 3 have marked hypertrophied musculature. This difference disappears in the veins of group 4 as the ratio of muscle to lumen of the normal group is 0.65 and compares favorably with the ratio in the hypertension group, which is 0.59 (table 1, fig. 8).

While this work was in progress, an article by Goldzieher and Sherman on the same subject appeared. They calculated, by measurement of diameters of the lumens and thicknesses of wall, the ratio of lumen to muscle in cases of hypertension and in cases of known normal blood pressure in fifty-one cases, selecting nine veins from each. They said, "The musculature of the suprarenal veins in cases of hypertension compares with that of the supra-

*By this expression is meant that the ratio was 1.5:1; and in each instance in this paper in which ratio is expressed by a single value it is understood that the other quantity, although unexpressed, is 1.

TABLE 1

RATIO OF AREA OF MUSCLE TO AREA OF LUMEN IN SUPRARENAL VEINS IN CASES OF ELEVATED AND NORMAL BLOOD PRESSURE

Blood pressure	Group 1 Lumen areas in sq. mm. less than 10	Group 2 Lumen areas in sq. mm. 10 to 19.9 inclusive	Group 3 Lumen areas in sq. mm. 20 to 29.9 inclusive	Groups 4 to 9 and 13 Lumen areas in sq. mm. greater than 29.9
Hypertension				
Lumen*	179.5	615.4	983.7	3216.7
Muscle*	286.0	537.4	976.5	1915.8
Number of veins	29	40	40	69
Ratio	1.5	0.87	0.99	0.59
Normal				
Lumen*	339.6	978.0	721.2	573.3
Muscle*	514.0	959.3	412.3	378.0
Number of veins	53	67	29	13
Ratio	1.5	0.97	0.57	0.65

*Aggregate areas in sq. mm.

renal veins in cases of normal blood pressure, as 4:1." The variation in the results of their study and of mine is doubtless due to the methods used.

The total lumen: Comparison was made of the total lumen area in the hypertension and in the normal groups. For this purpose, the total lumen of all veins with and without musculature was calculated separately in sections 1, 2, 3 and 4 (fig. 1) in each of the hypertension and normal groups. The average was determined in each case by dividing the total lumen area by the number of sections studied. The results are shown in table 2 and figure 9. The hypertension suprarenal glands are markedly more highly vascularized by veins than are the normal glands. Thus, considering the various sections 1, the average lumen area is 1.8 times as great in the hypertension suprarenal gland as in the normal gland; in sections 2, it is 1.9 times as great, in sections 3, 2.5 times as great, and in sections 4, 1.6 times as great. One must conclude from these data that the total area of the venous channels, as defined in this paper, in the glands in cases of hypertension was markedly increased over that in the glands in cases in which the blood pressure was normal. A small portion of this increase may be due to the greater size of the glands, as Philpot reported. He studied twelve specimens in one group, five from cases of mild hypertension and seven from cases in which it was assumed that there was hypertension. The average weight of the suprarenal glands was 12.4 gm. There were three specimens in the second group, all from cases in which it was assumed that there was low blood pressure. The average weight of the suprarenal glands was 7.7 gm. These data are entirely inconclusive due to the small amount of material studied. I approached the problem of differences in

TABLE 2

DEMONSTRATION OF INCREASED VASCULARIZATION OF SUPRARENAL GLANDS BY VEINS IN SECTIONS OF GLANDS FROM CASES OF HYPERTENSION AS COMPARED WITH SECTIONS REMOVED FROM SAME AREAS OF GLANDS IN CASES OF NORMAL BLOOD PRESSURE

	Sections 1	Sections 2	Sections 3	Sections 4
Total lumen area in square millimeters				
Hypertension	3230	3111.2	1453.7	325.9
Normal	2262.7	1341.2	468.5	606.8
Number of sections				
Hypertension	28	21	12	3
Normal	37	18	10	9
Average lumen area in square millimeters				
Hypertension	115.3	148.1	121.1	108.6
Normal	61.1	74.5	46.8	67.5
Ratio of average lumen area (hypertension) to average lumen area (normal)	1.8	1.9	2.5	1.6

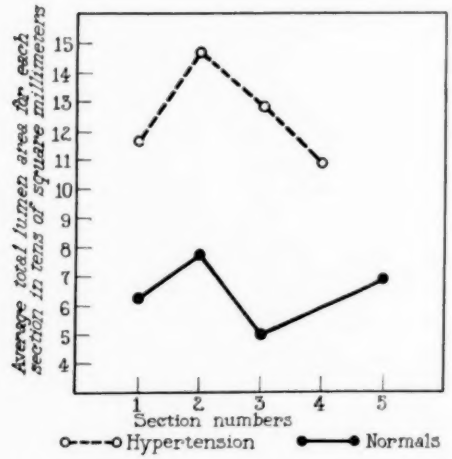

FIG. 9. Comparison of the vascularization by veins of sections of suprarenal glands in cases of normal and high blood pressure. The glands in cases of hypertension are more highly vascularized.

the size of glands in the two series of cases by measuring with the planimeter the surface area of the sections studied. There seems no question but that the glands in the hypertension series are larger (table 3). The increased size is, however, entirely inadequate to explain the increased vascularity.

The percentage of veins with muscle: Three hundred and thirty veins from cases of hypertension were studied; of these 178 (53 per cent) had musculature as defined in this paper. Of 372 veins from cases in which the blood pressure was normal, 160 (43 per cent) possessed musculature. This series is too small to justify a definite conclusion, but it is probable that the additional 10 per cent of hypertension veins developed muscle—as a reaction to the same factors which produced hypertrophy.

Anatomy and Physiology

The close connection between the abdominal sympathetic system and the suprarenal glands has been well described by Latarjet and Bertrand. In the main, there are two pedicles, the posterior and the internal. The former is composed of a considerable number (often more than twenty) of nerve threads. The internal pedicle comes from the solar plexus and is composed of larger fibers which terminate at the lower part of the internal border of the suprarenal gland. The fibers which constitute this pedicle are very numerous. Each suprarenal gland receives not less than thirty-three sympathetic nerve filaments. The close relation of the medulla of the gland to the sympathetic ganglia has been emphasized (Kohn,[30] 1902, Wiesel,[57] 1904, and Biedl,[6] 1913). Elliott[15] has said, "The ganglion cell and the adrenal cell are as brother and sister to one another, born of the same stock, living for the same end in life, which the one attains by growing out into direct contact with the mass of moving muscle, while the other stays quietly where it was born and exercises its influence from a distance."

The blood supply to the suprarenal gland is profuse; it receives from eleven to twenty-one branches from the phrenic accessory, lumbar and renal arteries and some from the ab-

Table 3
Comparison of the Areas of Sections of Glands from Cases of Normal and Increased Blood Pressure

	Group 1	Group 2	Group 3	Group 4*
Number of sections				
Hypertension	26	23	13	3
Normal	18	14	9	3
Ratio of average section area hypertension series to normal series	1.3	1.2	1.2	1.4

*Too few sections to be of value. The glands from patients who had hypertension are larger. The results are vitiated somewhat by irregular shrinkage of the glands.

dominal aorta direct. The distribution of blood vessels within the gland has been described by Flint. Neumann, Stewart and Rogoff, Burton-Opitz and Edwards have shown that rate of blood flow through the glands is extremely high. The results of these various experimenters show a blood flow as great as 7 c.c. for each gram of organ each minute, or as little as 2.2 c.c. for each gram of organ each minute, and they give the general impression that the rate of flow is greater than in any other structure of the body. Cow demonstrated that blood may pass from the suprarenal gland directly into the kidney and vice versa and suggested that epinephrine may exert some direct control over the kidneys. Elman and Rothman demonstrated venous reflux from suprarenal gland to kidney following ligation of the main venous channels away from the suprarenal gland.

The increased liberation of epinephrine from the gland, as a result of stimulation of the abdominal sympathetics, has been noted by many physiologists (Cannon and Lyman, Stewart and his collaborators, Dreyer, Tscheboksaroff, and others). Cannon believes the conclusion justified that "the adrenal secretion is under control of the thoracico-lumbar autonomic (sympathetic) system." He demonstrated the effect of emotion on the liberation of epinephrine. The pupils of the eyes of a frightened cat became dilated, there is inhibition of movement of the stomach and intestines, increased rate of heart beat and erection of hairs of the back and tail; all of these phenomena are signs of nervous discharges along sympathetic paths, indicating widespread subjugation of the viscera to control of the sympathetic nervous system. These physiologic reactions may be induced by the injection of epinephrine. In fact, epinephrine has been called the mimic of the sympathetic nervous system. Cannon demonstrated increased release of epinephrine under conditions of fright. He believed that the persistence of the emotional state, after the exciting object had been removed, could possibly be due to the effect of the epinephrine originally released, which had returned to the gland after traveling through the circulation and further stimulating the release of epinephrine. Stewart and Rogoff showed that epinephrine was released almost immediately, a fraction of a second, following stimulation of the splanchnic nerves.

Comment

The increased vascularization by veins, as defined in this paper, in cases of hypertension is significant. I believe it indicates increased functional activity of the suprarenal glands in cases of hypertension, since there is probably increased vascularization by arteries as well.

The cause of hypertrophy of the musculature of the veins in the suprarenal gland is possibly a subject for conjecture. Three chief theories of what the hypertrophy indicates present themselves: (1) increased functional activity of the suprarenal gland, (2) increased activity of the general sympathetic nervous system, or (3) a reaction to noxious substances in the blood stream.

Increased functional activity of the suprarenal gland: Although the supra-

renal gland probably secretes products other than epinephrine, the uncertain nature of them makes it necessary to include only epinephrine in this discussion. It should be borne in mind, however, that any other products liberated in the blood stream are subject to the same mechanism to which epinephrine apparently is subject. The mechanism by which epinephrine is expelled from the suprarenal gland is unknown. Neither Cannon nor Rogoff was able to give me information on this subject. The rapidity with which it is released suggests a physical mechanism. As early as 1897, Biedl[5] had shown that the splanchnic nerves convey vaso-dilator impulses to the gland. The longitudinal masses of muscle of the veins in the suprarenal gland have no direct vasoconstrictive effects, because of their peculiar placement. Contraction of these masses would shorten the veins, and probably would increase the diameter*. This would create an area of temporarily lowered intravascular pressure, into which epinephrine would rush from sinuses containing a high concentration of epinephrine if it can be assumed that such concentrations are present. Surely the time of appearance of increased epinephrine in the venous blood following splanchnic stimulation, a fraction of a second, precludes the more or less passive physiologic extrusion of the product of the cells and indicates that stores of increased concentrations of the secretion are called on and delivered quickly, probably by some simple mechanism. The contraction of the longitudinal masses of muscle furnishes the most obvious explanation. Goormaghtigh and Elaut, however, believe the suprarenal gland is for emergency function, all the material being stored in advance and the blood routes being ready to augment the exchange surface. Hypertrophy most commonly indicates overwork and there is some logic in the supposition that the hypertrophied musculature in cases of hypertension indicates an increase in the liberation of epinephrine. Goldzieher and Sherman believed, however, that contractions of these muscles in cases of hypertension might occlude the normal channels of venous drainage of the gland and force the venous flow back through the kidney and liver. Its effect might then be primarily on the kidney and secondarily on the systemic blood pressure.

The well known vasoconstrictive effects of epinephrine long ago led to the hypothesis that hypertension was due to hyperepinephrinemia. As early as 1904, Vaquez postulated increase in the function of the suprarenal glands in cases of chronic interstitial nephritis. Aubertin and Ambert, in 1904, examined the suprerenal glands from eight patients who had suffered from contracted granular kidneys, with increased blood pressure, and found hyperplasia or adenoma of the cortex in seven. Josué, Widal and Ménétrier made similar observations. Wiesel[58] made examinations in twenty-two cases of chronic interstitial nephritis with increased arterial tension and long-standing cardiac hypertrophy; in all,

*Henderson has shown that when two veins anastomose the bundles of muscle on the adjacent sides fuse in the angle of union. As shown in his diagram, contraction of the longitudinal muscles would produce active dilatation of the vein.

he found hyperplasia of the chromaffin substances in the medulla of the suprarenal gland. Parkinson made examinations in fourteen cases of high blood pressure and found an increase in the chromaffin substances in all but three. Philpot made examinations in twenty-two cases, in nineteen of which the diagnosis had been chronic interstitial nephritis and in three of which hypertrophy of the left ventricle had been present, without chronic interstitial nephritis. He found that the medulla was increased in size and that there was an increased quantity of chromaffin substance. He concluded, "These investigations tend to show that, besides the usual factors associated with, or causing high blood pressure, a condition of increased activity of the suprarenal glands, or hyperepinephrinism, is very often, if not invariably, present." The finding of increased vascularization by veins in the present study might well indicate increased functional activity of the suprarenal glands in cases of hypertension. Elliott[15] was not of this opinion for in his Sidney Ringer memorial lecture he said, "I could find no justification for the belief that the adrenalin cells are hypertrophied or more active in diseases associated with a persistent increase in blood pressure." Oppenheimer and Fishberg found cortical adenomas in five out of thirty cases of hypertension and only in one out of fifty cases without hypertension. They reviewed the literature and found nine cases of suprarenal tumors, derived from the cortex, associated with hypertension or with cardiac hypertrophy supposedly due to hypertension. From two of the patients concerned (Volhard), hypernephromas had been removed and the hypertension had disappeared. These authors found in the literature reports of five cases in which there were tumors of the chromaffin substance. In one patient, the tumor was associated with essential hypertension and in one with paroxysmal hypertension; one patient did not have hypertension and two had only anatomic evidence of increased blood pressure. These authors added one case to the few reported in the literature, that of a youthful patient with a blood pressure of 220 systolic and 160 diastolic, in which necropsy revealed a tumor of the suprarenal cortex. Neubauer, Oppenheimer and Fishberg found increased blood sugar in eleven cases with hypertension and felt that this constituted some evidence that the amount of epinephrine in the blood was increased; however, they could not eliminate sclerosis of vessels of the pancreas as the cause. C. H. Mayo reported a case of paroxysmal hypertension in which the blood pressure was reduced to normal by removing a tumor which possibly originated in the sympathetic nervous system or in the suprarenal gland. Goldzieher and Molnár were able to demonstrate an increased amount of epinephrine in suprarenal glands from cases of hypertension. As recently as 1928, Goldzieher and Sherman demonstrated hypertrophy of the musculature of the veins in cases of hypertension and concluded, "Our results add new and weighty evidence to the theory which links hypertension and allied diseases with functional disturbances of the suprarenal glands." These observations and opinions suggest the constant

but increased liberation of epinephrine as a cause of hypertension. Such a condition has no experimental foundation, for, according to Markowitz, "In the experimental animal sufficient epinephrine to cause hypertension is enough to raise the blood sugar to an extreme diabetic level, dilate the pupils, paralyze intestinal and gastric movement and cause erection of hair along the neck and tail." Obviously these conditions do not exist in the human being with hypertension. Cannon and Lyman have further shown that small amounts of epinephrine injected into the cat cause a fall in blood pressure, a result which they explained on the basis of the state of muscle: "relaxed when tonically shortened, contraction when relaxed." Janeway, in 1913, carried out numerous pharmacologic experiments with the blood of patients with essential hypertension. He concluded that the hypothesis that hyperepinephrinemia is a cause of hypertension was not supported by his results and characterized such a theory as a "beautiful dream." Ingier and Schmorl were unsuccessful in an attempt to demonstrate increased amounts of epinephrine in the suprarenal glands of individuals with hypertension. The technic described by Schur and Wiesel for demonstrating epinephrine in the blood has not withstood criticism. Recently Mosenthal has reviewed the evidence of hyperepinephrinemia as a cause of hypertension. He said: "This idea has been categorically affirmed and denied by any number of observers, but definite proof of an excess activity of the suprarenal gland has not been furnished. The very presence of epinephrine in the blood, thus far, has not been demonstrated and the successful quantitative estimation of this substance has not been accomplished." The theory of hyperepinephrinemia as a cause of hypertension is at present subject to discussion. The rôle of epinephrine cannot be dismissed, however, without consideration of the effects of countless episodes of liberation of epinephrine over a period of years. The vasopressor effects of subcutaneously injected epinephrine are as short as two minutes. Markowitz has advanced evidence that epinephrine is destroyed in the walls of the blood vessels, an observation which agrees well with the known effects of repeated injections of epinephrine on the structure of blood vessels. Is it not possible that there is present a condition of localized activity of the sympathetic nerve supply to the suprarenal gland* which releases numerous spurts of epinephrine over a period of years? As a result of the destruction of epinephrine in the walls of the vessels and overwork due to the greatly increased activity of vasoconstriction and vasodilation, may not anatomic changes occur in the systemic arteries? And may not hypertension be a direct result of these changes?

Increased activity of the sympathetic nervous system: The extremely close anatomic and physiologic connection between the sympathetic nervous system and the suprarenal gland has been emphasized. The same physiologic association between the general arterial system and the sympathetic nervous

*Such a condition of localized sympathetic hyperactivity is present in Raynaud's disease.

system is well known. Stated simply, stimulation of the sympathetic system causes increased blood pressure by virtue of widespread vasoconstriction, and the same stimulus simultaneously causes impulses to be transmitted probably to the muscular walls of the veins of the suprarenal gland and probably causing them to contract. Hypertrophy of the muscles of these veins in all probability indicates increased functional activity, which occurs as a result of sympathetic overactivity. Changes in the musculature of the veins might then be an index to changes in the muscular coats of the arteries of the general systemic circulation, since both changes probably are of the same origin, that is, sympathetic overactivity. This opinion has some physiologic and clinical confirmation. Cannon showed increased liberation of epinephrine in the experimental animal under conditions of fear, asphyxia and pain. This is brought about by sympathetic activity, probably generalized, since Stewart and Rogoff have shown that the liberation of epinephrine is entirely controlled by the abdominal sympathetics. It seems likely that the same conditions as those induced under experimental circumstances are present in many human beings. In this modern age, with the greatly multiplied difficulties of living and adaptation to environment, there are numerous daily episodes of sympathetic stimulation as a result of emotional changes. This hypertrophy of the muscles of the veins of the suprarenal gland, as well as that of the systemic arteries, may be simply an expression of heightened susceptibility to external stimuli in individuals subject to hypertension. This muscular hypertrophy may mean that the sympathetic nervous system is worked twice as hard in patients with elevated blood pressure and that the musculature has become twice as great in all vascular structures supplied by sympathetic nerves. Numerous observations on individuals in whom high blood pressure has been developing at the time of the observations have shown that there is an early stage of unknown duration, probably of many years, during which the blood pressure will descend to normal or nearly to normal under proper conditions of rest. This is the "functional" stage of hypertension. Later this condition does not obtain; the blood pressure is more firmly fixed at a high level, of which Elliott[14] has said, "It pursues its life history undeviatingly." Is this not the sequence of events: (1) numerous stimuli to the sympathetic nervous system of a hypersusceptible individual, with vasoconstriction and a brief increase in blood pressure in response to each stimulus (functional hypertention), (2) hypertrophy of the musculature of all vascular structures supplied by the sympathetic nervous system as a result of these countless episodes of constriction and relaxation, and (3) fixed hypertension as a result of this hypertrophy? Elliott[14] has supported this view of widespread vascular overwork as brought out in the first of the sequence of events just suggested: "May it not be as good a surmise as any other that essential arterial hypertension is in its inception a vascular neurosis, that certain individuals possessing certain susceptibilities in their vascular responses transmitted by inheritance pass into a state

of vasomotor susceptibility as middle life approaches?"

If this theory of the neurogenic origin is tenable, the hypertrophy of the musculature of the veins could be explained as a direct result of increased activity of the general sympathetic nervous system. Certainly venous hypertension is not a factor, for the systemic intravenous blood pressure is not increased in cases of hypertension until the myocardium begins to fail. It seems justifiable to conclude that the pressure within the suprarenal veins is of similar value to that in the general venous circulation. The short time between the occurrence of failing myocardium and the demise of the patient, with the fact that the intravenous pressure never becomes great, would seem to exclude increased intravenous pressure as the cause of muscular hypertrophy in the suprarenal gland. Here is an interesting condition: on the one hand is increased intraarterial pressure (hypertension) with muscular hypertrophy in the arterial walls; on the other hand, normal blood pressure within the veins, and yet muscular hypertrophy of the veins. If the muscular changes in the systemic arteries and the suprarenal veins have the same origin (overwork), this is evidence that the hypertrophy of the arterial walls precedes or occurs concomitantly and does not follow the increased arterial tension, since there is no hypertension within the veins where similar muscular hypertrophy is present. Does this not indicate that we must hold with reservation the view that arterial muscular hypertrophy occurs as a result of hypertension? It seems more probable that the muscular changes are cause and not effect of fixed hypertension.

Reaction to noxious substances in the blood stream: I have shown previously the shortcomings of the theory of constant hyperepinephrinemia as a cause of hypertension and I believe with Janeway that it is a "beautiful dream." The hypothesis of numerous episodes of liberation of epinephrine must be entertained with reservation. The theory of sympathetic overactivity as reaction to strain seems applicable in a large group of cases, but it fails to explain hypertension in children and in those phlegmatic individuals who apparently are free from abnormal responses to emotional stimuli. It may be reasonable in these instances to believe that there is widespread vascular hypertrophy, due to the effect of substances circulating in the blood stream, and that they produce their insidious effects on the venous and arterial walls, in a manner completely divorced from the emotional reaction of the patient. Is it not probable that hypertension is the physiologic answer to these changes in the walls of the vessels? This conception of the mechanism must rest on the findings of comparable changes in all other vascular structures with musculature. Unfortunately this information is not available. I found some evidence against it in my study as only the veins of intermediate size of the suprarenal glands participated in the process of muscular hypertrophy. It is difficult to understand why the other veins would be missed in a process due to a circulating toxic substance. Further study is needed. Comparatively too much attention has been given the study of

the small arteries of the systemic circulation, and far too little to veins. Particularly too little attention has been paid to the vessels of the pumonary circulation where the nature of these changes is not complicated by increased blood pressure within the lumens. The study of the veins of the suprarenal gland avoids the factor of increased intravascular pressure, but the profuse supply of sympathetic fibers adds confusion. The pulmonary circulation should furnish excellent material for study, as here the intra-arterial pressure is increased little or none and vasomotor fibers are entirely or almost entirely absent. I hope to make such a study the basis of a future report.

Conclusions

1. Veins of the suprarenal gland, the individual areas of the lumens of which in cross sections are between 19.9 and 30.0 sq. mm. have, in cases of hypertension, a ratio of muscle to lumen twice as great as that in cases of normal blood pressure. Theoretically, this hypertrophy indicates the following: (1) increased function of the suprarenal glands, (2) overactivity of the sympathetic nervous system, or (3) the effect of noxious substances in the blood stream.

2. The total area of the lumens of all veins, as defined in the paper, is greater in cases of hypertension than in cases of normal blood pressure. This shows that there is a higher degree of vascularization in the former which probably indicates a higher level of functional activity.

3. These observations are distinct evidence of a close relationship between increased functional activity of the suprarenal glands and hypertension.

Bibliography

[1]Abel, J. J.: On epinephrin, the active constituent of the suprarenal capsule and its compounds. Am. Jour. Physiol., 1898-1899, ii, iii-iv.

[2]Addison, Thomas: On the constitutional and local effects of disease of the suprarenal capsules. Works, London, The New Sydenham Society, 1868, 211-239.

[3]Aldrich, T. B.: A preliminary report on the active principle of the suprarenal gland. Am. Jour. Physiol., 1901, v, 457-461.

[4]Aubertin and Ambert: Quoted by Philpot.

[5]Biedl, Arthur: Die Innervation der Nebenniere. Arch. f. d. ges. Physiol., 1897, lxvii, 443-483.

[6]Biedl, Artur: Innere Sekretion. Berlin, Urban and Schwarzenberg, 1913, 692 pp.

[7]Brown-Séquard: Quoted by Elman and Rothman.

[8]Burton-Opitz, R. and Edwards, D. J.: The vascularity of the adrenal bodies. Am. Jour. Physiol., 1917, xliii, 408-414.

[9]Cannon, W. B. and Lyman, Henry: The depressor effect of adrenalin on arterial pressure. Am. Jour. Physiol., 1912-1913, xxxi, 376-398.

[10]Cow, Douglas: The suprarenal bodies and diuresis. Jour. Physiol., 1914, xlviii, 443-452.

[11]Cybulski and Szymonowicz: Quoted by Flint.

[12]Dakin, H. D.: The synthesis of a substance allied to adrenalin. Proc. Roy. Soc. London, 1905, s. B, lxxvi, 491-497.

[13]Dreyer, G. P.: On the secretory nerves to the suprarenal capsules. Am. Jour. Physiol., 1898-1899, ii, 203-219.

[14]Elliott, A. R.: Essential hypertension. Am. Jour. Med. Sc., 1927, clxxiv, 244-259.

[15]Elliott, T. R.: The adrenal glands. Brit. Med. Jour., 1914, i, 1393-1397.

[16]Elman, Robert and Rothman, Philip: Adrenal insufficiency and atrophy of the cortex following venous obstruction of the suprarenal glands. Johns Hopkins Hosp. Bull., 1924, xxxv, 54-58.

[17]Flint, J. M.: The blood-vessels, angiogenesis, organogenesis, reticulum, and histology of the adrenal. Johns Hopkins Hosp. Rep., 1900, ix, 153-228.

[18]Von Fürth, Otto: Zur Kenntniss der brenzcatechinähnlichen Substanz der Nebennieren. Ztschr. f. physiol. Chem., 1898-1899, xxvi, 15-47.

[19]Fulk, M. E. and MacLeod, J. J. R.: Evidence that the active principle of the retroperitoneal chromophil tissue has the same physiological action as the active principle of the suprarenal glands. Am. Jour. Physiol., 1916, xl, 21-29.

[20]Gley: Quoted by Pende.

[21]Goldzieher, M. A.: Quoted by Goldzieher and Sherman.

[22]Goldzieher, M. and Molnar, B.; Beiträge zur Frage der Adrenalinämie. Wien. klin. Wchnschr., 1908, xxi, 215-217.

[23]Goldzieher, M. A. and Sherman, Irving: Hypertrophy of muscle in suprarenal vein in hypertension. Arch. Path. and Lab. Med., 1928, v, 1-12.

[24]Goormaghtigh, N. and Elaut, L.: Le plan de structure de la surrénale au point de vue physiologique. Compt. rend. Soc. de biol., 1925, xcii, 733-735.

[25]Hartman, F. A.: The production of epinephrin by the adrenal cortex. Science, 1923, lviii, 74.

[26]Henderson, E. F.: The longitudinal smooth muscle of the central vein of the suprarenal gland. Anat. Rec., 1927, xxxvi, 69-78.

[27]Inger, Alexandra and Schmorl, Georg: Über den Adrenalingehalt der Nebennieren. Deutsch. Arch. f. klin. Med., 1911, civ, 125-167.

[28]Janeway, T. C.: Nephritic hypertension: Clinical and experimental studies. Am. Jour. Med. Sc., 1913, cxlv, 625-656.

[29]Josué: Quoted by Philpot.

[30]Kohn, A.: Chromaffine Zellen; chromaffine Organe; Paraganglien. Prag. med. Wchnschr., 1902, xxvii, 325-329.

[31]Kohn: Quoted by Bailey, F. R. and Miller, A. M.: In: Text-book of embryology. Ed. 4, New York, William Wood and Co., 1923, p. 399.

[32]Langlois, P.: L'altération fonctionnelle des capsules surrénales. Arch. d. physiol. norm. and pathol., 1897, s. V, ix, 152-167.

[33]Latarjet, A. and Bertrand, Pierre: Recherches anatomiques sur l'innervation des capsules surrénales, des reins et de la partie supérieure de l'uretere. Lyon chir., 1923, xx, 452-462.

[34]Lewandowsky, M.: Wirkung des Nebennierenextractes auf die glatten Muskeln der Haut. Centralbl. f. physiol., 1900, xiv, 433-435.

[35]Markowitz, J.: Personal communication.

[36]Mayo, Charles: Paroxysmal hypertension with tumor of retroperitoneal nerve. Jour. Am. Med. Assn., 1927, lxxxix, 1047-1050.

[37]Ménétrier: Quoted by Philpot.

[38]Mosenthal, H. O.: The relation of blood sugar to blood pressure. Am. Jour. Med. Sc., 1928, clxxvi, 761-769.

[39]Neuman, K. O.: The oxygen exchange of the suprarenal gland. Jour. Physiol., 1912, xlv, 188-196.

[40]Neubauer, Ernst: Über Hyperglykämie bei Hochdrucknephritis und die Beziehungen zwischen Glykämie und Glucosurie beim Diabetes mellitus. Biochem. Ztschr., 1910, xxv, 284-295.

[41]Oliver, G., and Schafer, E. A.: On the physiological action of extract of the suprarenal capsules. Jour. Physiol., 1894, xvi, i-iv.

[42]Oppenheimer, B. S. and Fishberg, A. M.: The association of hypertension with suprarenal tumors. Arch. Int. Med., 1924, xxxiv, 631-644.

[43]Parkinson, P. R.: The activity of the suprarenal glands in relation to blood pressures. Tr. Path. Soc. London, 1907, lviii, 187-199.

[44]Pende, Nicola: Has adrenin any physiological value in the organism? New York Med. Jour., 1923, cxviii, 469-475.

[45]Philpot, Austin: An investigation into the histological condition of the suprarenal glands in conditions associated

with a high blood pressure. Quart. Jour. Med., 1909-1910, iii, 34-51.

[46]Robertson, H. E.: Personal communication.

[47]Schur, H. and Wiesel, J.: Ueber eine der Adrenalinwirkung analoge Wirkung des Blutserums von Nephritikern auf das Froschauge. Wien. klin. Wchnschr., 1907, xx, 699.

[48]Stewart, G. N.: Adrenal insufficiency. Endocrinology, 1921, v, 283-306.

[49]Stewart, G. N. and Rogoff, J. M.: The spontaneous liberation of epinephrin from the adrenals. Jour. Pharmacol. and Exper. Therap., 1916, viii, 479-524.

[50]Stewart, G. N., Rogoff, J. M. and Gibson, F. S.: The liberation of epinephrin from the adrenal glands by stimulation of the splanchnic nerves and by massage. Jour. Pharmacol. and Exper. Therap., 1916, viii, 205-245.

[51]Takamine, J.: The isolation of the active principle of the suprarenal gland. Proc. Physiol. Soc. London, 1901-1902, p. xxix.

[51]Tscheboksaroff, M.: Über sekretorische Nerven der Nebennieren. Pflüger's Arch. f. d. ges. Physiol., 1911, cxxxvii, 59-122.

[53]Vaquez: Quoted by Philpot.

[54]Volhard: Quoted by Oppenheimer and Fishberg.

[55]Wheeler and Vincent: Tr. Roy. Soc. Canada, 1917, xi, 25.

[56]Widal: Quoted by Philpot.

[57]Wiesel, Joseph: Zur Pathologie des chromaffinen Systemes. Virchow's Arch. f. path. Anat., 1904, clxxvi, 103-114.

[58]Wiesel: Quoted by Oppenheimer and Fishberg.

Relation of Syphilis and Yaws*

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IT is doubtful if any other disease has influenced more materially the destinies of the human race than has syphilis. No other human disease punishes ignorance so unerringly and unmercifully as does this one, for it is the only human disease which is commonly carried over from parent to child congenitally.

It is certain that for thousands of years mankind has been aware of the fact that this disease was often transmitted by sexual intercourse and it was the stigma of shame, attached to this fact, which made him try to suppress all notice of the disease. For centuries since the renaissance which brought into the open truths of all kinds, facts about this disease have been suppressed and attempts have been made by the learned, who should have known better, to place the origin of syphilis to the credit of any other race of people than that to which the particular wise man who was doing the writing about it, belonged. When Columbus discovered America, the wise ones of the old world saw their chance to escape from the stigma in a body, so they placed the disgrace upon the Carib Indians with whom he first made contact and the Great Discoveror, has ever since, been credited with having introduced syphilis into Europe upon his return there from his first voyage to Hispaniola. The fallacy of this has been pointed out by such masters in medicine as August Hirsch, Sir Wm. Osler, Karl Sudhoff, and many others so that it is difficult to understand why any one at this time should subscribe to it. This would not be mentioned except to drive home the lesson, that we of 1929 who are so bold and frank in writing popularly concerning other sex matters are still sulking in the dark when it comes to giving out facts about syphilis in the public prints and we physicians are still clinging to the mediaeval folly. In a personal communication Dr. Judson Daland told me recently that "the word 'syphilis' never appeared in English in the newspaper until about ten or fifteen years ago, and almost never appears in any magazine or newspaper today, although Edward Bok used the term in the Ladies Home Journal when he printed articles on the evils of venereal diseases."

It is paradoxical that our young people should know so much about sex psychology and Freudianism and so little about the facts of syphilis, a dis-

*Lecture and lantern demonstration given to the class in tropical diseases at Georgetown University Medical School, May 3, 1929.

ease peculiar to the human species which has influenced so materially the welfare of man since first he made his appearance upon the earth.

In describing what we mean by Yaws of Frambaesia, we will first give three definitions of the term in order that you may better understand: The first is that of Sauvages who briefly described it in 1768 and was, I believe, the first author to use the term "frambaesia" as a synonym for it. His work "Nosologia Methodica" is remarkable for its accurate description of diseases of every type. Nosologia may be said to sum up the medical knowledge of that day very accurately. Those of my hearers who have ever attempted to get an exact picture of the best knowledge obtainable upon any subject or specialty for any generation of the past, will understand what I mean when I say that Sauvages' work acts as a "point of departure" for the medical knowledge of 1750, just as that of Sydenham did for 1650 and that of August Hirsch did for the period 1850 to 1880. The following is a translation of Sauvages' Latin definition of Yaws. "Frambaesia; Yaw of the People of Guinea; Epian or Pian of the Americans, is a contagious disease endemic in Guinea and in the Americas, *sometimes congenita*[1] as shown by Father Labat* with the Caribs, the principal symptom of which is the frequent eruption of mushroom-like growths with the color and shape of the raspberry, whence the African name yaw, because it sounds like frambaesia; to these symptoms are added eating ulcers, exostoses, caries, ankyloses and emaciation."

The second definition is that of the 9th Edition of the popular work of Manson-Bahr on Tropical Diseases just now off the press: "Yaws is a contagious inoculable disease, characterized by an indefinite incubation period, and followed usually by fever, by rheumatic-like pains, and by the appearance of papules which generally develop into a fungating, encrusted, granulomatous eruption. Running a chronic course, it is mostly protective against a second attack. The disease is caused by *Treponema pertenue*, and is controlled by salvarsan and certain bismuth salts."

The third conception is one which the speaker has committed to words, but this view regarding Yaws has been held for several hundred years and so taught by such great physicians as Thomas Sydenham and Jonathan Hutchinson. Here it is: "Yaws is epidemic non-Venereal syphilis transmitted innocently amongst primitive peoples and under stone-age conditions of personal hygiene constitutes one of the exanthemata of childhood. It is then called yaws, frambaesia, pian, bubas and so on variously according to the race and language of those affected."

With the lantern we will show you examples of most types of the so-called yaws and will in many instances show parallel conditions in "orthodox Caucasian syphilis." From the last definition you will at once infer that yaws is a disease of the unwashed and ignorant. It is not wholly a disease of the dark-skinned races of man, as syphilis of the innocent has often been

*Jean Baptiste Labat, 1663-1738, 1694-1705, in French colonies. Noveaux Voyage aux isles d l'Amerique, 1724.

described in epidemic form for primitive whites. In the present state of civilization we find, however, that those primitive conditions which foster yaws are found mostly in the tropics and amongst the dark-skinned and the dirty. It is the most important of present day diseases which are confined rather strictly to the tropics.

If this definition is correct, the reverse of it should be demonstrable, and that we believe is capable of proof beyond question. To state this reverse proposition categorically, we will say that treatment, civilized clothing, shoes and habits change epidemic syphilis to venereal syphilis or "civilization syphilizes yaws." It makes an innocently acquired disease come to be a venereally acquired one.

The paradox of an actively contagious condition disappearing from certain islands and countries while maintaining its full reign in nearby islands or adjacent countries in close communication with the first, finds its only logical and satisfactory explanation in the above assumption. In Haiti syphilis is the city disease, yaws in its florid state is confined mostly to country districts. Of course, I do not mean to say that yaws is *never* venereally acquired. Doubtless a father or mother often acquires venereal syphilis and when the infective mouth or eruptive lesions are fullblown, the children of the household acquire "Yaws" innocently from this first case. No treatment being administered to any of them the whole infected family tails off into latent or tertiary syphilis, gangosa, goundou or juxta-articular nodes and no man knoweth "whence it cometh and whither it goeth." Verily the ways of the *Treponema* are dark and devious, its manifestations protean and serious.

African slavery began for the New World in 1517 when Bartholomé de Las Casas, afterwards bishop of Chiapa (1544) intervened at the court of Spain on behalf of the oppressed Indians of Haiti. He advised Charles V to permit each Spanish resident of the New World Colonies to import twelve African slaves. This first legalized slavery in America but a few African slaves had been imported into Haiti as early as 1502. In order to understand the speaker's explanation of Yaws and its wide prevalence, present and past, in the West Indies, it is essential to keep in mind the above historic facts, as well as the following: The Portuguese first began to explore the west coast of Africa as early as 1442. This was 55 years before Vasco de Gama rounded the Cape of Good Hope (the date was November 20-22, 1497) and fifty years before Columbus discovered the New World. Because of these West African discoveries the Portuguese made agreements with other contemporary Governments which gave them control of the slave traffic from West Africa for many years. During the 300 years following 1520 many millions of slaves were imported into the Americas from Africa. It is our belief that the Portuguese infected the "Slave-bearing" fringe of Africa with their venereal type of syphilis and that the 75 years of their contact with this coast through the slave trade before they began sending slaves to America was sufficient to give the negroes Portuguese syphilis. The negroes interpreted the white-man's syphilis in

terms of yaws and when the West Indian slave trade began, passed it back to him as such. This type we know was brought over in the slave ships from the earliest history of this deplorable traffic. Oviedo writing as early as 1529 assures us that what we now know as Yaws was present in Haiti at that time and that it was the same disease as in Europe was known as the French disease, the Neapolitan disease, etc. He remarks that in Europe it was known to be a disease of prostitutes and the lowest class of society.

Thomas Sydenham, known as the British Hipprocrates who lived between 1624 and 1689, wrote about this disease and he interprets it almost exactly as did Sauvages 100 years later. He describes it thus: "But to me it rather seems to have taken its rise from some nation of the Blacks upon the borders of Guinea for I have been informed by several of our countrymen of great veracity, who lived in the Caribbee islands, that the slaves which are newly from Guinea, even before they land, and likewise those that live there, are afflicted with this disease, without having known an infected woman; so that it frequently seizes whole families, both men, women and children. And, as far as I can learn, this disease, which so frequently attacks these miserable people, does not at all differ from that we call the venereal disease, with respect to the symptoms, viz, the pains, ulcers, etc., allowing for the diversity of climates; tho' it goes under a very different name, for they entitle it the Yaws. Nor does their method of cure differ from ours, for in both cases a salivation raised by quicksilver carries off the disease; notwithstanding what we say here of the excellent virtue of guaiacum and sarsaparilla in those places where they grow, which is judged to be nearly lost in their long passage to us."

In his accurate observations of the findings in "Parangi" which is the name for Yaws in Ceylon, Sir Aldo Castellani in the summary to his paper reporting spirochaetes in this disease uses the following words, "In 7 of 11 cases of Parangi spirochaetes have been found. Of these spirochaetes there is an extremely delicate variety, which in my opinion, is absolutely identical (sic) with the Spirochaete pallida (sic) of Schaudinn. If my hypothesis should be proved to be wrong, a proper name for the organism might be S. pallidula."

This was only a few weeks after Schaudinn and his co-workers had described *Treponema pallidum* and correspondence with this investigator developed the fact that Schaudinn's organism and that discovered by Castellani were indistinguishable morphologically. I might add that up to May 3, 1929, they are still indistinguishable not only morphologically but by any other means known to science.

It is impossible within a reasonable time to discuss each point of this question. But suffice it to say that evidence is at hand which would convince the open-minded investigator that Yaws is just syphilis which is operating under slightly different conditions of transfer from individual to individual. The identity can be proven as far as it is possible to prove anything in medicine by tests and studies old and new, arranged under the fol-

lowing heads, any one of which might occupy from a half minute to a half day depending upon the state of "openness" of the particular mind to accept facts. This statement presupposes that the individual to be convinced knows a reasonable amount about the different aspects of syphilis. These headings are (1) Etiology (2) Immuniology (3) Clinical Course (4) Epidemiology (5) Pathology (gross and microscopic) (6) Prophylaxis (7) Treatment (8) History.

We may best define the attitude of those who contend that Yaws is anything else than syphilis in these words. They have taken a few symptoms of the protean disease we know as syphilis and define this collection of symptoms under the name of Yaws. All those cases of the larger symptomatology which do not come within this small group they call syphilis.

We may draw a parallel from what obtains in plague. It is just as if we should say that flea-borne bubonic plague were the only real plague and that the droplet-borne pneumonic plague is not plague at all because it is generally communicated in a different way.

To those irreconcilables we recommend an unbiased study of the isolated population of Guam. This island has been in frequent communication with the white man ever since Magellan discovered it in 1520, that is to say for 409 years. A study of this population in relation to the infection under consideration will make unnecessary any animal experimentation to determine the identity of yaws and syphilis. The answer is given by correct reasoning upon the facts observed and recorded for this unintentional but very definite human experiment. In other words the answer is a matter of logic and not of "highbrow science."

Editorials

OUR CONFUSED CONCEPTIONS OF CHRONIC ARTHRITIS

As pointed out by J. Alison Glover in his report to the British Ministry of Health, chronic arthritis is no new disease, being equally as prevalent in the prehistoric dwellers of Nubia and Upper Egypt as in the Saxon forefathers of the Heptarchy. It occurs in the lower animals as frequently as in man. Accurate observations upon gout are found in the Hippocratic writings; and the 29th aphorism, Book VI, is as true today of the women of England as of the Greek women of the Archipelago in the Fifth Century, B. C. In the Third Century, B. C., Erasistratus employed modern hydrological methods, graduated exercise, diet and vapour baths in the treatment of joint affections. The following centuries contain little or no reference to the disease, and it was not until the time of Sydenham that chronic rheumatism of a form, incurable and lasting as long as life itself, was first described in medical literature. Sauvage, in his "Nosologica Methodica" (1763) divided gout into fourteen forms and rheumatism into ten. His *arthritis rheumatica,* or *goutte rhumatismale,* is most probably identical with the rheumatoid arthritis of the present day. To Sauvage's attempts at classification of arthritic conditions we probably owe much of the present day confusion attending chronic arthritis. In 1795, Cullen made the first atempt to simplify this elaborate classification by recognizing only acute and chronic forms. Landre-Beaurais in 1800 differentiated the *"goutte rhumatismale"* of Sauvage under the term of *"goutte asthenique primitive."* In 1829, Gruveilhier made the first definite differentiation of *osteoarthritis* as an individual entity under the designation of *"chronic rheumatic arthritis."* Adams, in 1831, applied the term *"malum coxae senilis"* to the monarticular form involving the hip joint. Scudamore had as early as 1827 emphasized the importance of the inflammatory changes in the periarticular connective tissues, to which Watson in 1843 again directed attention. Bright and Addison gave in 1839 their sanction to the use of the term *"rheumatic gout"* for chronic arthritis. Fuller (1852) divided rheumatic diseases into three chief divisions: *acute rheumatism* (*rheumatic fever*), *muscular rheumatism* (including sciatica and brachial neuritis), and *rheumatic gout* (including what is now termed rheumatoid arthritis and osteoarthritis). Garrod (1858) used the term *"rheumatoid arthritis"* to cover all forms of chronic arthritis save gout, on the assumption that what we now call rheumatoid arthritis and osteoarthritis are but different aspects of the same disease. Charcot agreed with Garrod in this view. The term *"arthritis deformans"* was introduced in

1860 by Virchow. Since that time confusion has resigned in the use of the three terms: rheumatoid arthritis, osteoarthritis and arthritis deformans, and this confusion of conception of chronic arthritis still holds in the medical literature of the day. The American Official Nomenclature makes rheumatoid arthritis a synonym for arthritis deformans. Hoffa and Wollenberg, in their work on "Arthritis Deformans," Stuttgart, 1908, take the exact opposite of this standpoint, and consider arthritis deformans a synonym of osteoarthritis, sharply distinguishing it from rheumatoid arthritis. An examination of the current standard textbooks shows the same confusion of usage. According to different authorities we may take our choice of views, as follows:—arthritis deformans includes rheumatoid arthritis and osteoarthritis as different forms of the same disease (McCrae); rheumatoid arthritis includes a periarticular form and osteoarthritis (Taylor, Carter and Gibson); osteoarthritis includes all the chronic joint diseases (International List); arthritis deformans is a synonym for rheumatoid arthritis and quite distinct from osteoarthritis (American Official Nomenclature); arthritis deformans is a synonym for osteoarthritis and quite distinct from rheumatoid arthritis (Hoffa); rheumatoid arthritis and osteoarthritis are entirely separate and distinct diseases (Hoffa, Hale White, Llewellyn Jones, and Garrod); or all the terms, arthritis deformans, rheumatoid arthritis and osteoarthritis are synonyms and indistinguishable (Encyclopedia Britannica). This last-named usage is probably the most common among English and American medical men of today; but the great variations in usage and standpoint make a serious situation, for one worker in the line of these diseases can never be sure that another in his own country or in a foreign country is using any one of these terms in the same sense that he is using it. Consequently the etiological and pathological basis of classification becomes hopelessly confused. Nothing is left for the individual observer but to put forth a new classification of his own. This has only served to increase the confusion, no one of the more recent classifications (Coates, Herbert, Strangeways, Fisher, etc.), based in part upon pathology and etiology, has helped to clear up this confusion. They have only served to emphasize the fact that a scientific classification of the many forms of chronic arthritis is not today possible, because of our ignorance concerning their etiology, pathogenesis and pathology. In attempting to clear up the situation, and to form a practical basis for the consideration of chronic arthritis diseases, the British Ministry of Health adopted in 1922 the following classification, to which it adheres in the present Report. This divides chronic arthritis into four groups: *Rheumatoid Arthritis* (including Infective Periarthritis); *Osteoarthritis* (including Malum Coxae Senilis); *Gout* and *Unclassifiable Chronic Joint Changes.* Rheumatoid arthritis usually begins with an acute attack of fever of considerable length; many smaller joints are usually affected, especially the 1st and 2nd phalangeal joints, spindle-shaped joints, and often involving the tempero-maxillary joint;

the changes are chiefly periarticular often accompanied by much fibrositis; the lesions are often bilaterally symmetrical; nutrition of patient is invariably bad; patients are usually females. The bone and joint cartilage usually escape obvious change in the first stage of the disease. The radiograph often shows little or no bony change. In the more chronic stages of the disease the formation of chondro-osteophytes occasionally produces lipping, but to a lesser degree and at a later stage than in osteoarthritis. All of the varieties of rheumatoid arthritis are at least three times more frequent in women than in men. The patients show a definite constitutional peculiarity, being chiefly of the asthenic, slender build, similar to that associated with tuberculosis. They usually show stigmata of a true toxemia in the form of a low continued fever, cold clammy hands and feet, inactive skin, pale bad complexion, poor appetite, and lowered general nutrition. The disease often begins with an initial attack of fever, which may closely simulate an attack of acute rheumatism, although the absence of any real reaction to sodium salicylate and the absence of the flitting from joint to joint and cardiac complications so characteristic of acute rheumatic fever, may help in the differential diagnosis, yet so close is the resemblance that the disease is often at first diagnosed and treated as acute rheumatism, the real diagnosis does not become apparent until the fever subsides. Then the patient finds that the joint inflammation persists instead of clearing up, her muscles waste, and pain, swelling and deformity remain. All forms of rheumatoid arthritis usually begin, more or less symmetrically in the smaller joints, especially the first and second joints of the fingers, and, by the swelling of the ligaments and the surrounding fibrous tissue, the finger-joints assume a characteristic spindle shape. The early involvement of the temperomaxillary joint is very characteristic, so much so that Herbert considers its presence, together with pain, stiffness and grating in the back of the neck, the "jaw-neck syndrome," as a basic test for rheumatoid arthritis. The larger joints become involved later, and at first there is little deformity, except for the spindle-shaped swelling of the fingers and other joints. Atrophy of the muscles takes place early, and is very noticeable; later, muscular spasm leads to deformity of characteristic type. The hands assume a position of palmar flexion with ulnar deviation. Many varieties of rheumatoid arthritis have been described by various authorities. One of these, a peculiarly acute and intractable form occurring in young women deserves especial mention. In this form the initial attack is usually severe and the resemblance to acute rheumatic fever especially close. Little or nothing is known of its etiology; a recognizable focus of infection is rarely seen associated with it. Is usually ends in the pathological form known as atrophic. Some American authorities (Goldwaite) term rheumatoid arthritis "atrophic arthritis" in contrast to hypertrophic arthritis, but most English writers reserve that term for that form in which there is a marked rarefaction of the bone (about 6 per cent.) *Osteoarthritis* is usually afeb-

rile, shows a gradual onset, often at first confined to one large joint, fewer and larger joints are affected, especially knees and hips. There is grating, lipping, eburnation and formation of osteophytes. The lesions are often asymmetrical, and the patient is usually well nourished. The first change in osteoarthritis is a degeneration of the articular cartilage, especially where the pressure of the opposing cartilage is greatest; the cartilage here undergoes a process known as fibrillation, which has been compared by French to the changes in the cataractous lens. Under the worn cartilage the bone becomes eburnated, dense and ivory-like, and at the outer edges of the joint, both cartilage and bone proliferate. For a comparatively long time the synovial membrane may be unaffected, but eventually that portion nearest the articular cartilage becomes villous. The proliferated bone and cartilage form first a "lipping," and eventually osteophytes. These may become detached as free bodies and yet continue to grow. It is peculiar to this disease that, at the same time, and in the same joint, there is going on at the same time both absorption and production of bone. The changes are slow, but gradually give rise to great deformity, very different from that due to rheumatoid arthritis. All the fibrous tissue about the joint may be ossified, or may soften and disappear, and the joint may even become dislocated. Clinically osteoarthritis shows usually an insidious onset, beginning with stiffness and creaking in one or more of the larger joints. It is much less symmetrical than rheumatoid arthritis. The general health and nutrition of the body are much less affected than in rheumatoid arthritis, and the disease is found especially in stout, well-nourished people. In the monarticular form of the disease, one large joint only, one knee, one hip, or shoulder is grossly diseased, but in this form too, it is usually possible to detect signs in other joints on careful search. Slight fever sometimes accompanies an exacerbation in one joint, but the course of the disease is, as a rule, free from fever. The skin in this affection is of normal color, even ruddy and warm, reacting well to external change. Osteoarthritis is throughout its course much more of a local or joint disease than is rheumatoid arthritis, which is so clearly a general systemic disease. The erosion of cartilage and the thickening of the synovial membrane give rise to a creaking and grating characteristic of the disease, and a sudden "locking" type of pain in the joint is also characteristic. The knee is most frequently involved (35 per cent in males, 55 per cent in females). In women the osteoarthritis of the knees so often seen between the ages of 45-55 forms a large part of the so-called *climacteric* arthritis. Some writers hold that osteoarthritis is but a different manifestation of the same disease as rheumatoid arthritis, others that it is but an end result of rheumatoid arthritis, while others claim that it is an entirely distinct disease. Fisher, who has made an extensive study of its pathology, says that it is not a disease *sui generis*, but is rather the series of physiological and pathological changes that ensue in a joint subjected to prolonged or oft-repeated injury, either mechanical or toxic, but of a moderate degree of

intensity. The usual text book description is accepted for *acute gout. Chronic gout* is regarded as a polyarthritis with a definite history of repeated attacks of acute gout or the presence of tophi. Under *chronic joint changes unclassifiable* are grouped those chronic joint changes which cannot be allocated to any one of the three preceding forms. About 15 per cent of all cases of chronic arthritis will have to be so relegated. In the recent Ministry of Health Inquiry 13 per cent of the chronic arthritis cases were thus classified. This British Report on Non-Specific Chronic Arthritis should be of special interest to American readers, because of the apparent increase in the number of patients showing various forms of the affection presenting themselves in American clinics, and, also, because of the growing importance of the physical therapy of these conditions in the joints. It is essential that each case of arthritis be given a thorough examination and carefully differentiated diagnosis, before physical therapeutic measures are instituted. What is urgently needed is more light upon the etiology, pathogenesis and pathology of joint affections in order to clear up the ambiguity attending their terminology. There is a tendency for these cases to collect in certain institutions and sanatoria. Wherever this is the case advantage should be taken of the situation in the provision of proper equipment for observation and diagnosis, as well as for the treatment, otherwise the latter tends to become too empirical.

Abstracts

A Report on Chronic Arthritis. With Special Reference to the Provision of Treatment. By J. Alison Glover, O.B.E., M.D., M.R.C.P., D.P.H. (Reports on Public Health and Medical Subjects, No. 52, Ministry of Health, London, 1928).

This is the third report submitted to the British Minister of Health concerning the public health and preventive aspects of the so-called "rheumatic" diseases. The first, published in 1924, dealt especially with the incidence of rheumatic diseases in adult insured persons; the second report, published in 1917, dealt with acute rheumatism in children in its relation to heart disease. For presentation in an official report few subjects could be more involved than that of chronic arthritis, because of its confused nomenclature and our ignorance of the exact causes and real nature of this condition. Yet while its etiology is still obscure its treatment is entering a more hopeful phase, and even in the existing state of knowledge there is much that can be done to prevent, to alleviate, and even to cure chronic arthritis which is not being done. Nonspecific arthritis is alone considered in this report; acute surgical arthritis, pneumococcal, scarlatinal, gonococcal, tuberculous, syphilitic, dysenteric, meningococcal, hemophilic arthritis and that due to injection of serum are excluded. Following the precedent of the previous report on Acute Rheumatism, the statements in the author's summary are not advanced as "conclusions" or as proved by the subject matter of the report. Our knowledge of the etiology and our experience as to the results of the treatment suggested are alike too limited and imperfect to permit of any "conclusions" in the strict sense. Nevertheless, his summary represents what, in the opinion of the writer, appears to be the present position. Chronic arthritis, while constituting a disease group that is inconspicuous as a cause of death and almost absent from in-patient hospital statistics, is nevertheless one of the greatest factors in the production of suffering and invalidity. It costs the community immense loss in time and work, and causes a drain upon the National Health Insurance funds amounting to at least one-fourteenth of the total sum paid in sickness and disablement benefit. Chronic arthritis affects chiefly persons of middle and old age, and except in the case of gout, women more than men. Rheumatoid arthritis, howeevr, usually has an earlier age of onset than the other forms of chronic arthritis, and begins more frequently between the ages of 20-30 than in any other age period. Its acute form often begins in girls under 20. The etiology of chronic arthritis is still imperfectly understood. It is probable that there are several important factors in its production. Of these factors, focal sepsis appears to be the chief, and there is definite evidence, more often than not, that it has played a leading rôle in the individual case; but diathesis, faulty metabolism, trauma, occupational stress, mental stress, senile change, and derangement of endocrinal balance seem all to be important factors. Unfortunately some of these terms are fully as ill-defined as is chronic arthritis, so that there is danger lest the explanation may seem to explain the unknown in terms of the unknown. In any case, it seems clear that chronic arthritis is a pathological condition which, like food poisoning or bronchitis, can be produced by a variety of agents or causes. This uncertain etiology gives rise to great difficulty in the classification of the several diseases in the group, and is the main cause of the wide variation in the use of the terminology. No satisfactory classification can be arrived at until more is known as to the etiology; but, apart from gout, two broad groups are distinguishable—namely, rheumatoid arthritis and osteoarthritis. The climacteric arthritis of

women at the menopause is considered by some sufficiently clear-cut to deserve a class to itself. Many systems of further subdivision have been devised, but none has received general consent. These fundamental uncertainties can only be cleared up by continuous and intensive study, from every viewpoint, of large numbers of cases of patients in the early stages of the disease. To this end an organization, which includes full facilities for assembling together sufficient patients, and for thorough diagnosis, careful records, complete equipment for early and adequate treatment, and an effective system of following up, seems essential. It would appear that to achieve such an organization the provision of one or more special "units" is necessary. A proportion of cases of chronic arthritis (amounting perhaps to 10 or 15 per cent, and including many of those acute cases which occur in comparatively young female patients) are exceedingly intractable to treatment of any kind. These cases have produced an impression, which still survives in many quarters, both professional and lay, that chronic arthritis is an incurable disease. On the other hand, whilst no specific remedy is known, it would seem that a much larger proportion, perhaps one-third of all cases, can be cured, and more than another third relieved to a greater or less extent by early, appropriate and skillful treatment. Far from chronic arthritis being incurable, there are few disease groups in which early and proper treatment is more necessary or more effective. The more important sites of focal infection associated with chronic arthritis are those connected with the teeth, tonsils, the accessory sinuses, the genito-urinary system and the bowel, the first two mentioned being by far the most frequent. The organism most frequently found in focal sepsis associated with chronic arthritis is the non-hemolytic streptococcus veridans. If there be a recognizable focus of infection in a patient suffering with chronic arthritis, the first indication of treatment is to remove it if it be removable; if not removable to drain or treat it. To undertake other treatment in the presence of an unremoved or untreated focus can only be correct treatment in certain very exceptional cases. The removal of the focus must be conducted with due regard to the age, resistance, and general condition of the patient, the possibility of the procedure being made worse temporarily by increasing absorption being borne in mind, as well as the risk of shock. Where extraction of teeth is necessary the utmost care in clinical and radiographical examination must be taken to insure, on the one hand, that only thoroughly incriminated teeth are removed, and, on the other, that no septic root or diseased bone is left behind. The question of focal sepsis having been thoroughly explored, treatment of many other kinds has to be considered, whether it be immunological, dietetic, physical or surgical, or by means of drugs. Any of these treatments, if correctly applied, may be of value in suitable cases, but in practice a combined treatment is generally used. To achieve success requires long experience with the subtleties of the syndrome and real familiarity with the intricate niceties of the treatment used. It demands also a masterful yet persuasive personality and great patience in the physician. Each case must be treated individually and on its own merits. Immunological treatment is of value in certain cases—specific treatment with autogenous vaccines, particularly in comparatively early cases, and non-specific protein therapy either in early cases where a focus cannot be determined or in older cases apparently at a standstill. Some authorities use non-specific protein therapy by preference in all cases in which immunological methods are indicated. Dietetic treatment, particularly in the shape of low caloric feeding, is useful with the more robust patients, especially those with osteo-arthritis and climacteric arthritis. Many patients with rheumatoid arthritis, on the other hand, require a generous diet, rich in vitamins B and D. Thyroid treatment is of service in certain cases. Physical treatment is of great value at some stage in almost every type of chronic arthritis. No scheme of treatment for chronic arthritis can be considered complete unless a large range of physical methods under skilled direction is provided. There is an urgent and rapidly increasing demand for physical treatment, which demand already far ex-

ceeds the provision, and which may increase very rapidly in the future as the education of the public in the value of such treatment increases. The most important forms of physical treatment for chronic arthritis are electrical treatment, including diathermy, radiant heat and ionization, massage and exercises, and the various forms of hydrological treatment. Hydrological treatment, if not an essential part of the physical treatment of chronic arthritis, is an invaluable adjunct. It is important for the resorption of inflammatory products, for the relief of pain, for the restoration of lost function in the joints and lost reaction in the skin, and for the reeducation of wasted muscle. Hydrological treatment has its fairest hope of success when given as spa treatment, i.e., when the patient can devote his whole time to the treatment in favorable surroundings, with the advantages of change of air and regimen, and in some cases the additional advantages of the specific therapeutic qualities of the natural waters of the spa. Many forms of hydrological treatment can, however, also be given with great benefit to patients, using ordinary waters at hospitals other than spa hospitals and at out-patient clinics. Physical and hydrological treatment involve special experience, specially trained staff, and special equipment, and these can only be secured economically if the treatment, as far as out-patients are concerned, be given in centers suitably equipped to deal with large numbers of patients. Such physical treatment centers (including, of course, the special out-patient departments of certain general hospitals) should also be arranged to act as clearing houses, directing patients as to the form of treatment particularly suited to their special need and the place where it may be obtained. Some cases need the removal of a focus of infection, some the intensive study of an arthritis unit, others are suitable for treatment at a spa or spa hospital, whilst others would be greatly benefited by regular out-patient treatment at the center. These centers should be organized in closest liason with the "arthritis unit" and with the spa hospitals, and should provide the continued supervision, observation and necessary after-care which should follow institutional treatment. Such centers would be of the greatest service in many conditions other than arthritis, notably fractures and injuries, deformities, fibrositis and diseases of the nervous system. For the necessary research into the etiology and into the relative and real values of methods of treatment an "arthritis unit" housed either in a large wing of a general hospital, or in a separate institution, is required. This unit should be situated near, and work in closest cooperation with, either a university or a large teaching school of medicine, which would enable it to fulfill the purposes of research and observation as well as of treatment. Here patients would come at the earliest stages of their disease for thorough examination by modern methods, for diagnosis and for record; here the focus of infection would be sought, and, if possible, found and removed; here the necessary bacteriological, biochemical and radiographical work could be completed before the patient was passed on to the spa hospital, or to the physical treatment center, or convalescent home, to complete his cure; here orthopedic surgery, or the fitting of the more elaborate appliances occasionally necessary in advanced cases, would be performed. In regard to preventive measures no directly prophylactic procedure can be urged, but many important indirect measures may be mentioned. Of these the recent development of dental benefit is probably one of the most important, following, as it does, the immense reduction of dental sepsis in children due to the school medical service. The prevention of dental caries is too large a subject to be discussed here, but the means available in the present state of our knowledge fall under four heads: (1) education of the people as a whole in the value of good teeth and the disadvantages of diseased teeth; (2) the supply of a proper diet adequate to promote the growth of perfectly formed and regular teeth; (3) instruction in the daily practice of oral hygiene, including the use of a detergent dietary; and (4) regular periodical dental inspection and treatment of the teeth. Pickerill advocates, in addition, that all meals should contain a fair proportion of salivary excitants, and, more important still, should both commence and end with some article of diet having

an acid reaction. The attention to tonsillar sepsis in the school medical service also seems likely to diminish the incidence of acute rheumatism in children. The increased attention to the question of lead solvency in water may be a factor in the reduction of gout, which seems to be in progress, and may perhaps be of service with certain forms of nephritis. The importance of the prevention of dampness in the sites of dwellings and in the dwellings themselves, and the importance of the free circulation of air and of sunlight about dwellings is probably great in the prevention of most kinds of arthritis. Dampness in a dwelling is an unmixed evil alike to the structure of the house and to the health of the inmates. The provision of pithead and works baths, and the proper first aid treatment of minor sepsis, are perhaps only slightly less important in the prevention of arthritis than in the prevention of fibrositis. Overeating or drinking, bad at any time, become destructive as we approach middle life—the period of chronic arthritis. Then there are important means of maintaining the muscular tone, and the skin reaction of the individual, as well as his resistance to disease. Bathing, sun bathing, games, sports, exercises—particularly those in the open air—are of the utmost importance in counteracting the evil effects either of sedentary occupation, or the special stress of occupational trauma. Then, too, are important the prophylactic effects of correct posture, and the prevention of postural and static deformities, scoliosis, flat feet and many another ill. "We grow old because we stoop, rather than we stoop because we grow old," says oen distinguished authority on physiotherapy. We must keep supple, "Not tied or manacled with joint or limb." Function is the important thing. The disordered function is the disease.

Reviews

What Every One Ought to Know. By OLIVER T. OSBORNE, M.A., M.D., F.A.C.P. 313 pages + XIV. Charles C. Thomas, Springfield, Illinois, and Baltimore, Maryland, 1929. Bound in green cloth. Price $2.50.

The object of this book is to present in simple language some of the truths concerning the wonderful mechanism of the human body and to outline some of the delicate physiologic processes which insure growth and maturity, and promote nutrition and health. To further the objective of "keeping well," nutrition, foods, exercise and general hygienic rules are discussed. The various infective causes of ill health are listed, and how they are acquired and the efficient measures of prevention are described. Chapters are devoted to the growth of children, to their mental and physical health and to their early school life. Some of the many accidents that occur to civilized people are discussed from the standpoint of the layman and his responsibility in giving first aid. The book is not intended to offer treatment for diseased conditions. Self-treatment is always of doubtful value and is frequently dangerous, often allowing a simple indisposition to develop into serious acute or chronic disease. The author sincerely hopes that the book will cause a better understanding of one's self and one's fellows, and that it will promote health and aid in preventing disease and its consequent unhappiness and even financial stress. The contents consists of seventeen chapters, as follows:—Growth and Development, Functions of the Body, Nutrition, Foods, Diet, Promotion of Health, The Mouth, The Child, Some Statistics, Exercise, Infection, Prevention of Disease, Habits, Accidents, Poisons, The Skin and Nostrums and Quackery. The material in these chapters is well chosen and expressed in good, simple language. It is distinguished for its safe and sane common sense. The reviewer notes with interest the author's views on the use of iodized salt and water for the general population, and wholly agrees with them. "Iodized salt is advertized. When these salts were first prepared they containd too much iodine and were not safe. Though containing less iodine at the present time, they still should not be used. One person eats much more salt than another, hence he would get much more iodine than one who ate but little salt. In other words, the dose of iodine in iodized salt can not be regulated. Iodized salt and iodized water supplies are not safe, as they may cause serious trouble with the thyroid gland. The prevention of goiter should be individual, and should be directed by a physician. It is not safe to iodize people by the wholesale or by city water supplies." With all of which we are heartily in accord. The writer shows a similar good common sense in his treatment of diet and nutrition. On the other hand he appears to be too much influenced by current fads of focal infection, especially as far as the teeth and tonsils are concerned. What scientific proof exists in the literature for the statement that "acute inflammation of the joints and acute disease of the heart most frequently start from the tonsils"? Surely such a flat statement as this cannot go unchallenged. The reviewer wishes that the author had shown the same conservatism of statement in this respect that he did in regard to iodized salt. On page 220, the reviewer notes the use of the expression "pusy inflammation," an example of incorrect spelling as well as of poor choice of terms. The same error is repeated on page 287. The author shows a curious one-sided view of the relative importance of habits. Under this chapter heading practically only two things are considered, Narcotic Drugs and Tobacco. Certainly much could have been said to the point with reference to alcoholism and various other habits of greater importance than these two. This book

contains much information of real value, but is very far from being the "complete health book" it is advertised to be. Notably among the important omissions is all reference to the reproductive function, with its various problems, light upon which the average human being needs most of all, and most earnestly seeks. Any book, pretending to be a health book in any sense of the word, which is as devoid of enlightenment upon this subject, as is this present volume, certainly fails of achievement. The venereal diseases are not even mentioned in the index. One has come to expect Health Books to be written by some propagandist or other of some especial fad or other. This book seems to be especially free from this taint, only a suspicion of which exists in the sections on coffee and tobacco. On the whole it is a safe book to put before the public which needs so much informing and instruction along health and disease lines. Yet the reviewer regrets that it could not have been made more complete, and written upon a broader view-point. The ideal book of health has yet to be written—probably never will be written—owing to the excessive fluidity and constant progression of the subject.

Clinical Aspects of Venous Pressure. Macmillan Medical Monographs. By J. A. E. Eyster, B.Sc., M.D., Professor of Physiology, University of Wisconsin; Associate Physician, Wisconsin General Hospital, Madison, Wisconsin. 135 pages, 7 illustrations. The Macmillan Company, New York, 1929. Price in cloth, $2.50.

While important advances have been made during the last two decades in the knowledge and clinical application of arterial blood determinations, the significance of venous pressure, on the other hand, has been greatly neglected. Although the latter does not appear to have the same degree of interest as the former in a number of more or less diverse clinical states, recent work has tended to emphasize its paramount importance in present or impending cardiac decompensation from any cause, or when there is reason to anticipate the possibility of this event during the course of several diseases. Venous pressure is the most direct indication that can be obtained clinically of the extent to which the heart is moving its load of blood from the venous to the arterial side of the circulatory system, and it exhibits changes which precede the development of other signs and symptoms when the heart fails to do this to the normal degree. By far the greater part of the clinical situation in cardiac failure is due directly to venous engorgement, exhibited as passive congestion in various organs, and as exudates from serous membranes. As such engorgement occurs, the venous pressure rises, to fall again as the engorgement is reduced or disappears. Venous pressure may therefore be said to represent not only the primary factor that underlies the symptoms and functional pathology of cardiac failure, but to be also responsible in large part for the physical signs accompanying it, namely: edema, congestion, cardiac dilatation and reduced urinary secretion. As the principal underlying factor in these conditions, and as the principal index of cardiac behavior, it is the most reliable and important single factor to know and to follow accurately when this clinical state develops, or when it is impending. Determination of venous pressure by the indirect method of vein compression is accurate, and can be readily and quickly carried out. tI requires no more experience in order to secure confidence and accuracy than arterial pressure determinations. Although this method has been available and its importance more or less evident for a number of years, it has had by no means widespread clinical use in this country or abroad. It is hoped that the present book, written primarily for clinicians, and to stress the clinical application of veous pressure, will stimulate an interest which can only make for a better recognition, understanding and treatment of cardiac decompensation. Since an understanding of normal conditions must precede the interpretation of abnormal states, a brief review and presentation of the present conception of the cause and significance of venous pressure is given, followed by a discussion of the altered state that exists in cardiac decompensation. The conception of this condition which is presented has come in many of its details only recently through a more thorough understanding of cardiodynamics,

especially in its relation to venous pressure. The reviewer is wholly in accord with the theses of the author's preface as presented above. Venous pressure is as important clinically, if not more so, than is a consideration of arterial pressure; and the one-sided view of circulatory conditions prevailing in our clinics has always seemed inadequate and based upon a too narrow viewpoint. It is true that the majority of our clinical cardiologists practically disregard venous pressure as an important adjunct in the determination of cardiac compensation and decompensation, relying wholly upon arterial pressure and general cardiac phenomena. While recently the study of the capillary bed has been shown to throw additional light upon the circulatory state, there has been too great a neglect of the study of the venous pressure in the obtaining of the complete picture of the circulation as a whole. The material of this book is presented in eight chapters and an introduction. In Chapter I the mechanics of venous pressure in the normal and its relation to cardiac activity is discussed; in Chapter II cardiac decompensation; in Chapter III methods; in Chapter IV venous pressure range in the normal individual and the influence of various factors; in Chapter V venous pressure in cardiac decompensation; in Chapter VI venous pressure in conditions other than cardiac failure; while clinical cases are discussed in Chapter VII; and a general summary and bibliography complete Chapter VIII. The book is well written, in a clear, scientific style, and contains much recent clinical information relating to the circulation. It is a valuable contribution to the science of cardiology and performs a very important function in bringing to attention the much neglected field of venous pressure.

Diseases of the Skin. By RICHARD L. SUTTON, M.D., Sc.D., LL.D., F.R.S. (Edin.), Professor of Diseases of the Skin, University of Kansas School of Medicine; Assistant Surgeon, U. S. Navy, Retired; Dermatologist to the Santa Fe Hospital Association; Dermatologist to the Bell Memorial Hospital, the Swofford Home for Children, The Nettleton and Armour Homes for the Aged; and Visiting Dermatologist to the Kansas City General Hospital. Seventh Edition. Revised and Enlarged. 1394 pages, 1237 illustrations and 11 colored plates. The C. V. Mosby Company, St. Louis, Missouri, 1928. Price in cloth, $10.00.

That a seventh edition of this work should have been called for within two years of the publication of the sixth speaks sufficiently strongly for its popularity. At the time of the publication of the sixth edition it was thought that a new impression once in every three years would be sufficient to take care of all future needs, but the continued indulgent reception of the work, together with the accumulation of a large amount of new and valuable material has rendered this plan impracticable. Several recently discovered diseases have been introduced, the descriptions of some of the older ones rewritten, and the importance of others, such as certain of the occupational dermatoses, and those relating to allergy, emphasized. An attempt has been made to discuss intelligently the latest developments in cutaneous therapy, and to recommend those agents known to be reliable and practical. Much that is of theoretical interest only has been omitted, since a textbook is no place for the discussion of experimental medicine. Owing to the increase in size, the author has endeavored to get rid of all obsolete matter and to condense the new material as much as is consistent with clarity. In order to further economize space, a considerable number of valuable references have had to be confined wholly to footnotes, as otherwise the volume would have been so bulky and unwieldy as to impair seriously its usefulness. All of the changes that have been made in this edition have greatly improved it, and the work as it now stands is the most complete and up-to-date textbook on dermatology published in English, and the best illustrated of any published in any language. The author has an especial facility for seizing upon the most salient features of the various conditions described, and for giving these features an unusual clarity of presentation. Hence its great value clinically. The various personal touches add to its efficiency of presentation, as well as greatly increasing their interest. The book

is unusually free from diffuseness; in a subject so complicated as dermatologic conditions with their apparent overlapping and difficult clinical defferentiation Dr. Sutton has been singularly fortunate in presenting the essential entity of each affection. The ability to do this constitutes an especial art of the dermatologist who is also naturally a teacher. The great richness in illustration constitutes another valuable feature of this book; and it is especially noteworthy that a large proportion of these are microscopical. Thus the relation between the clinical appearance and the pathologic changes underlying these is made clear. We heartily recommend this textbook as one of the most efficient and effective textbooks on dermatology that has yet appeared.

College News Notes

COMMITTEE ON NOMINATIONS FOR 1929-30

In accordance with the amended By-Laws of the College, Persident John H. Musser, on April 25, appointed the following Committee on Nominations for the year 1929-30: W. Blair Stewart, Chairman, Atlantic City, N. J.; E. B. Bradley, Lexington, Ky.; James S. McLester, Birmingham, Ala.; J. H. Means, Boston, Mass.; Charles F. Martin, Montreal, Que. The By-Laws provide: "He (President) shall appoint within one month after induction to office a Nominating Committee of five, composed of two members of the Board of Regents, two members of the Board of Governors and one Fellow at large, whose duty it shall be to nominate candidates for the elective offices, Board of Regents and Board of Governors. The selection of the nominees for the Board of Governors shall be made after due consideration of suggestions of members from the respective states, provinces or districts which will be represented by the nominees, if elected. The list of nominees for President-elect and for the 1st, 2nd and 3rd Vice-Presidents shall be submitted to all the Masters and Fellows of the College at least one month before the Annual Meeting, and the election of all nominees shall be by the members of the College at its annual business meeting. This does not preclude nominations made from the floor at the annual meeting itself."

Dr. Leon Thayer Stem (Fellow), Chattanooga, has been elected President for 1930 of the Tennessee State Medical Association. From an editorial in the Journal of the Tennessee State Medical Association, it is stated that "Dr. Stem is one of the leading Internists of Chattanooga. . . . He is a man of good judgment, has a high sense of justice, and has always shown an interest in upholding the traditions of medicine. . . . In selecting its President for 1930, the Tennessee State Medical Association has followed the spirit of our country, which selects its leaders and honors those whose ability and determination make for them a place of leadership."

Dr. Oliver T. Osborne (Fellow), New Haven, is the author of a new book entitled "What Everyone Ought to Know," published by Charles C. Thomas, Springfield, Illinois. The book is on health and how to preserve it.

At the 32nd Annual Session of The American Gastroenterological Association held at Atlantic City, New Jersey, May 6th 7th, Dr. Frank Smithies, Chicago was elected President.

In the June, 1929, issue of *Annals of Internal Medicine*, page 1359 of the News Notes Section, reference was made to Dr. George R. Minot having resigned as head of the Medical Service of the C. P. Huntington Memorial Hospital during March, which by inference would be taken to be 1929. His resignation took place March 1, 1928.

Dr. George R. Minot (Fellow), Boston, addressed the Massachusetts Medical Society on June 12 on the subject, "Treatment of Anemia." He addressed the Maine State Medical Society at Poland Springs, Maine, June 18, on the same subject.

During Commencement week, Dr. Minot was eelcted an honorary member of the Harvard Chapter of the Phi Beta Kappa. He also received the Kober Medal of the Association of American Physicians on May 8, 1929.

Dr. P. P. McCain (Fellow), Sanatorium, N. C., was selected by a special Committee of the Moore County Medical Society for the award of the annual medal for 1928 for his paper on "The Diagnosis and Signifi-

cance of Juvenile Tuberculosis." The Committee's report states that they gave careful consideration to papers recommended by the sub-committees from each section. This Committee grades each paper, taking into consideration original work and other regulations adopted by the House of Delegates.

Dr. Gerald B. Webb (Fellow), Colorado Springs, as guest of honor at the Omaha meeting of the Nebraska State Medical Association, May 14-16, delivered an address entitled, "Early Diagnosis of Pulmonary Tuberculosis."

At the Tenth Annual Meeting of the Medical Staff of the Mt. Sinai Hospital, of Chicago, Dr. Maurice Lewison (Fellow) was elected permanent honorary President.

Dr. Allen K. Krause (Fellow), for several years associated with the Johns Hopkins Unievrsity Hospital, has accepted the Directorship of The Desert Sanatorium and Institute of Research, Tucson, Arizona. While Dr. Krause has already assumed many of the responsibilities of the post, he will probably not take up his resident duties until early fall. Dr. William Paul Holbrook (Fellow)is acting as Associate Director of The Desert Sanatorium and Institute of Research, and Dr. Charles W. Mills (Fellow) is Acting Medical Director.

Dr. William Fitch Cheney (Fellow), San Francisco, is President of the Commonwealth Club of California for 1929.

At the 32nd annual meeting of The Washington Medical and Surgical Society held at Washington, D. C., May 4th, Dr. Frank Smithies, Chicago, was the guest of honor and delivered the Annual Address upon the subject, "Intestinal Protozoiasis as Clinically Manifested in the Temperate Zone." Dr. Smithies was elected honorary member of the Society.

Dr. Hans Lisser (Fellow), San Francisco, is Vice-President of the California Academy of Medicine, Councilor of the Association for the Study of Internal Secretions, Chairman of the Executive Committee of the San Francisco County Medical Society, Associate Clinical Editor of *Endocrinology* and a Governor of the American College of Physicians.

At the 32nd Annual Session of The American Gastro-Enterological Association, held at Atlantic City, N. J., May 6-7, 1929, Dr. Frank Smithies, Chicago, donated a fund with the object of the Association's securing annually a guest speaker of national prominence in research work. The proceeds of the fund assure an honorarium to the invited guest of $100.00. This annual address is to be known as "The Walter C. Alvarez Lecture."

"Dr. James M. Anders (Master) received the honorary degree of Doctor of Laws from the Pennsylvania Military College on June 19, 1929, on the occasion of the Annual Commencement of that Institution."

The President-elect of the American Medical Association, elected at the Portland Session, Dr. William Gerry Morgan, was born in Newport, N. H., May 2, 1868. He received his A.B. degree from Dartmouth in 1890 and his M.D. degree from the University of Pennsylvania in 1893. After postgraduate work, he began practice in Southport, Conn., in 1894, and then removed to Washington, D. C., in 1899. In Washington, Dr. Morgan early made a place for himself in various medical and social activities. He became professor of diseases of the digestive tract in Georgetown University and has held that position since 1904. He was chairman of the Advisory Draft Board in the district during the World War and also lieutenant in the Naval Reserve Corps. Dr. Morgan has held positions in many medical organizations, serving as chairman of the Executive Committee of the American College of Physicians, as president of the American Gastro-Enterological Association, as president of the Clinico-Pathological Society. He is also a member of the American Therapeutic Association and of the New York Academy of Medicine. In the American Medical Association, Dr. Morgan was for several years a member of the House of Delegates.

Dr. L. J. Moorman (Fellow), Oklahoma City, delivered an oration entitled "Social Aspects of Tuberculosis" before the Thirty-seventh Annual Session, Oklahoma City, May 29, 1929.

Dr. T. H. McCarley (Fellow), McAlester, Okla., addressed the General Session of the Oklahoma State Medical Association, May 29, on "Keep the Well Baby Well."

Dr. Kenneth M. Lynch (Fellow), Charleston, S. C., was chosen president-elect of the American Society of Clinical Pathologists which met at Portland during the annual meeting of the American Medical Association.

Dr. David Riesman (Fellow), Philadelphia, Pa., addressed the Central Tri-State Medical Convention at Portsmouth, Ohio, on May 16.

Dr. Lyell Cary Kinney (Fellow), San Diego, Calif., was elected president of the California Medical Association during its meeting in San Diego on May 12.

Dr. Willard C. Stoner (Fellow), Cleveland, attended the American Medical Association meeting at Portland, Ore., where he discussed the "Chaos of Institutional Drug Therapy and Patient Management" before the section on Pharmacology and Therapeutics, after which he is touring the West, visiting hospital clinics and making a trip into Alaska.

Dr. Joseph H. Barach (Fellow), Pittsburgh, Pa., was elected Medical Director of the Falk Clinic. Falk Clinic is the outpatient department of the Medical Center, University of Pittsburgh. Plans for the clinic building have been approved, construction to begin at once. The clinic will have a working capacity of about 750 patients daily.

Dr. E. Roland Snader, Jr., (Fellow) is the author of an article "Hypothyroidism," which appeared in the March issue of the Hahnemannian Monthly.

Dr. Carl V. Vischer (Fellow) of Philadelphia, was elected a Visiting Physician to St. Luke's Hospital, at a meeting of the staff on February 23, 1829.

Dr. Linn J. Boyd (Fellow) of New York City is the author of an article, "Gastric Carcinoma" which appeared in the March issue of the Journal of the American Institute of Homeopathy.

Dr. Carl V. Vischer (Fellow) of Philadelphia is author of an article, "Instructions for the Tuberculous Patient Relative to Prevention," which appeared in the May issue of the Medical Searchlight.

The following Fellows of the American College of Physicians are members of the International Committee of the American Institute of Homeopathy which sailed from Montreal for Europe on June 27: Dr. G. Morris Golden, Philadelphia; Dr. Henry I. Klopp, Allentown, Pa.; Dr. Linn J. Boyd, New York City. The committee will meet with the British Homeopathic Medical Society in London, with the French National Homeopathic Society in Paris and with the German National Homeopathic Organizations in Berlin and Stuttgart.

Dr. C. Lydon Harrell (Associate), Norfolk, Va., was elected President of the Norfolk Medical Society on June 3 for the succeeding year. This society has a membership of 178 physicians from Norfolk, Portsmouth and surrounding territory.

Dr. Samuel A. Locwenberg (Fellow) of Philadelphia is author of a book "Diagnostic Methods and Interpretations in Internal Medicine" published by F. A. Davis Company, Philadelphia, Pa.

Dr. Karl V. Vischer (Fellow) of Philadelphia was elected a Vice-President of the Alumni Association of Hahnemann Medical College, Philadelphia, at the annual meeting on June 6.

Proceedings of the International Assembly of the Inter-State Post-Graduate Medical Association of North America, Atlanta,

Georgia, Session October 15,19, 1928, was edited and published for the Association by Dr. Edwin Henes, Jr., (Fellow) of Milwaukee, Wisconsin. The book contains essays by the following Fellows of the American College of Physicians; Dr. Lewellys F. Barker, Baltimore; Dr. Walter A. Bastedo, New York City, Dr. A. S. Warthin, Ann Arbor, and Dr. Harlow Brooks, New York City.

Dr. Arthur C. Morgan (Fellow) of Philadelphia and Dr. Lewellys F. Barker (Fellow) of Baltimore, Md., are members of the committee on the "Cost of Medical Care" whose chairman is Dr. Ray Lyman Wilbur.

At the 41st Semi-Annual meeting of the Eleventh Councilor District Medical Association held at Huntington, Indiana, May 16th, Dr. Frank Smithies, Chicago, was the guest of honor. Dr. Smithies conducted a morning clinic at The Huntington County Hospital and in the afternoon addressed the society upon "A New Physiological Method for the Examination of Patients Affected with Intestinal Stasis."

RESOLUTIONS

Passed by the Council of the Chicago Roentgen Society, June 24, 1929

WHEREAS, the storage and preservation of used x-ray films has recently become an economic and insurance problem, and

WHEREAS, the reports of the roentgenologists responsible for the diagnoses are of decidedly more value and importance than the films, and

WHEREAS, these reports are filed with, and become a part of the records of each case, making it unnecessary that large numbers and quantities of old and used x-ray films be preserved and retained for long periods of time, it is therefore

RESOLVED, by the Council of The Chicago Roentgen Society, acting officially for The Chicago Roentgen Society, that it is the sense and judgment of this Society, that it is not necessary to preserve any x-ray films for a longer period than two years after their exposure, and that in all cases where there is no likelihood of legal proceedings—such as ordinary clinical cases, medical conditions, gastro-intestinal and urinary tract examinations—it is deemed unnecessary to preserve or retain the x-ray films for a longer period than six months after their exposure.

This is, however, not in any way to be construed as discouraging the preservation of films of specially interesting or unusual conditions, as these are to be preserved because of their value for comparative study and for teaching purposes; and it is further

RESOLVED, that referring physicians desiring to preserve the x-ray films of their own patients, be encouraged to do this, and it is hereby declared permissible and proper practice for roentgenologists to deliver the films to the referring physicians in such cases; and it is further

RESOLVED, that a copy of these Resolutions be sent to The Bulletin of The Chicago Medical Society, The Illinois Medical Journal, The Journal of the American Medical Association, Radiology, and the American Journal of Roentgenology, for publication, and to the American College of Radiology, the American College of Surgeons and the American College of Physicians with request that the same be published in their official journals, and to the Sections on Radiology of the American Medical Association and of the Illinois State Medical Society, and to the Chief of the Fire Prevention Bureau of Chicago and the Underwriter's Laboratories, Inc., of Chicago, and to the editors of Hospital Management and Modern Hospital.

OBITUARY

Dr. James Winfield Cokenower (Associate), Des Moines, Iowa, died April 16, 1929, of pneumonia; aged 75.

Dr. Cokenower graduated from the Keokuk (Iowa) Medical College in 187, and later received the medical degree also from the Kentucky School of Medicine (Louisville) in 1882. He later did postgraduate study at the Kentucky University Medical Department.

Hospital. He was an ex-president of his County Medical Society, a member of the Iowa State Medical Association and a member of the American Medical Association. He had been an Associate of the American College of Physicians since 1925.

Dr. Cokenower was ex-professor of orthopedics at the Drake University College of Medicine (Des Moines), and formerly on the staffs of the Iowa Methodist Hospital and the Mercy Hospital. He was an ex-president of his County Medical Society and a member of the American Medical Association. He had been an associate of the American College of Physicians since 1925.

"Charles Stanley McVicar (Fellow), Rochester, Minnesota, died June 29, 1929, of coronary sclerosis; aged 49 years.

Dr. McVicar was born in MacGillivray Township, Middlesex County, Ontario, attended the public and high schools in Ailsa Craig and Parkhill. At the age of nineteen, he enlisted with the Canadian forces for service in South Africa. On his return to Canada, he entered the Western Medical College, where he studied for two years, from 1902 to 1904. The last two years of his medical course were taken at the University of Toronto Faculty of Medicine, where he was graduated as Silver Medalist in 1907. On completion of his hospital training, he engaged in practice in Toronto and was associated with the teaching staff of his Alma Mater.

During the World War, Dr. McVicar again served with the Canadian forces, this time in Salonika, where he was mentioned in dispatches for distinguished service by General Milne. He also served as Lieutenant Colonel, and as Chief of Medicine in the Orpington General Hospital, England. From here he was called to Toronto to take charge of the Christie Street Orthopedic Hospital, which was the central orthopedic institution of the Canadian Army.

In January, 1921, Dr. McVicar accepted an invitation to join the Staff of the Mayo Clinic. Owing to his outstanding ability, he was soon made head of a section in Gastro-enterology and Associate Professor of Medicine, The Mayo Foundation, Graduate School of the University of Minnesota.

His broad viewpoint in medicine, his firm, sincere and fearless character, likeable personality, his love of home and capacity for friendship marked him for leadership. He was an excellent speaker and was in great demand for medical meetings throughout the United States and Canada. He was a member of the American College of Physicians since 1926.

(Submitted by Dr. George E. Brown, Rochester, Minn.)

Edgar Orrin Crossman (Fellow), Washington, D. C., died June 21, 1929, at his summer home in Bedford, N. H., of pneumonia; aged 62 years.

Dr. Crossman was born at Ludlow, Windsor County, Vermont, attended the common schools at Plymouth, Vt., spent two years at the New Hampshire State College, and received his medical degree from the University of Vermont in 1887. Early in his practice he began to specialize in internal medicine and neuropsychiatry. He was in charge of the Department of Nervous

Diseases at the Clifton Springs (N.Y.) Sanatorium from 1891 to 1894; medical director of the Markleton (Pa.) Sanatorium from 1899 to 1903; medical director of the Lake View Sanatorium (Burlington, Vt.) from 1916 to 1918; and more recently had been appointed medical director of the U. S. Veterans Bureau.

Dr. Crossman had always been interested in keeping abreast of all developments in medical science, as evidenced by his pursuit of several postgraduate courses at such institutions as the New York Postgraduate Medical School, Harvard Medical School, Boston Psychopathic Hospital and the University of Michigan. He contributed a number of articles to various medical journals, and served as President of the New Hampshire State Medical Society. He was also a Fellow of the American Medical Association, a member of the Hillsboro County Medical Society, a member of the American Psychiatric Association, and was elected to Fellowship in the American College of Physicians on April 8, 1929. He further held the commission of Lieutenant Colonel in the Medical Reserve Corps of the U. S. Army.

"Caution, courage, acumen, and honesty were the outstanding characteristics of Dr. Crossman's character. He was lovingly called "the old fox." Such strength of character was never more needed in any position than when Dr. Crossman was directed to take charge of the Medical Service of the United States Veterans Bureau in 1924. He brought and gave to the Bureau not only mind and courage, but sound medical training and great technical knowledge. The Medical Bulletin of the Veterans' Bureau was published by his order. Without money, he installed the spirit of research into a half hundred hospitals. He fought for recognition of and proper recompense for the doctors under him. He instituted schools for the better training of his physicians. He constantly strove to have these physicians maintain the high ideals of the medical profession. His conception of the prime function of the Director of the Veterans Bureau was to secure for the doctors in the field both the men and materials required for their work. Thus he raised the Veteran's Bureau's hospitals above mediocrity. He was active in creating and most adroit in using the Director's Medical Council. He was untiring in devising ways to improve the Medical Service, but worked hardest to maintain those improvements which had been inaugurated. He was a great leader. His best thoughts seemed so simple and direct that they were not always recognized as great. Thousands of lives have been saved and other thousands have been improved by his foresight and wise administration."

(Submitted by Dr. Kennon Dunham, Cincinati, Ohio.)